सीबीएमआर
CBMR

ISSN No: 2582-9459

# 2020-21

# वार्षिक प्रतिवेदन
# Annual Report


जैव चिकित्सा अनुसंधान केन्द्र
Centre of BioMedical Research

Professor Alok Dhawan, Director, CBMR apprising the Hon'ble Chief Minister, Uttar Pradesh regarding translational work being done at CBMR and its future plans

# वार्षिक प्रतिवेदन
# Annual Report

(2020-2021)

सीबीएमआर CBMR
जैव चिकित्सा अनुसंधान केन्द्र
Centre of BioMedical Research
(An autonomous Centre under the Government of Uttar Pradesh)
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# Editorial Committee



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ISSN No: 2582-9459

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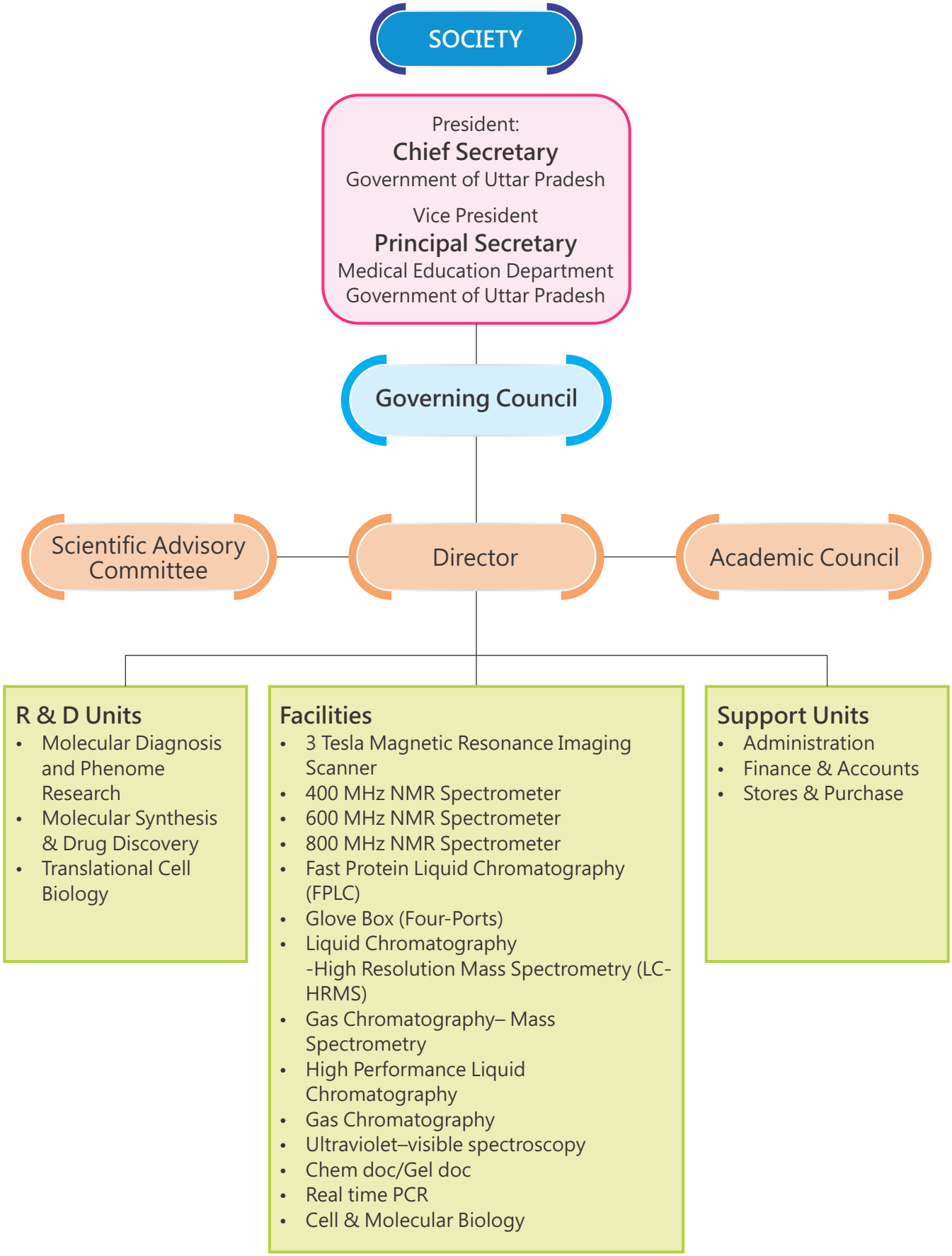
# ORGANISATIONAL STRUCTURE



# From the Director's Desk

It gives me pleasure to present before you the Annual Report 2020-2021 of the Centre of BioMedical Research (CBMR), an autonomous Centre of the Government of Uttar Pradesh. The Centre has fully functional advanced molecular biology, NMR, fMRI and chemistry labs to nurture cutting-edge research in various areas of basic, applied and translational aspects of biology and chemistry.

Some of the highlights of the scientific achievements in the reporting period include a series of powerful catalysts and ligands synthesized to solve a challenging and long-standing problem of introducing boron functionality onto the organic molecules. These catalysts and ligands can easily be synthesized and would certainly find wide application in the context of drug diversification, medicinal chemistry as well as in the pharmaceutical industries. Notably, these results were published in the Journal of the American Chemical Society (J. Am. Chem. Soc. 2021, 143: 5022–5037). Considering the impact of this work and new avenues it can open, the Editor of Journal Science wrote a piece "Better boron placement" [Science, 2021, 372 (6544): 804-805]. The identification and characterization of two new NADPH dependent anthrol reductases from fungus T. islandicus, were reported which are used for the stereo- and regioselective reduction of anthrols to obtain putative biosynthetic precursors. For the first time, the anthrol reductases have been applied towards the chemoenzymatic synthesis of several natural products including highly complex flavoskyrins and bisanthraquinones with implications on their biosynthesis [Organic Letters, 2020, 22: 8511–8515; Chemical Communications, 2020, 56: 3337–3340]. The work in ChemComm has been highlighted as Editor's Choice in Natural Product Synthesis Collection by the Royal Society of Chemistry (UK).

Employing NMR based metabolomics approach, a complex serum metabolic signature for predicting the severity of acute respiratory distress syndrome (ARDS) was identified. Further, using high-sensitivity solid-state NMR experiments, the short- and long- range interactions of collagen proteins inside bone matrix have been measured for its future applications in the clinical assessment of bone diseases. The whole brain functional connectivity in attention deficit hyperactivity disorder (ADHD) children and the pattern of functional brain changes in ADHD children using the resting state fMRI technique was studied. This will help in the early diagnosis of ADHD children, and also to adopt early rehabilitation measures for ADHD children. Another fMRI study on deaf patients revealed critical imaging parameters that will help in assessing the ideal patients for the cochlear implant as well as monitoring the outcome after the cochlear implant. These studies are of immense clinical significance and will help in better patient care.

It gives me immense satisfaction that in the recently published Institutional rankings by Nature Index (2020-21), CBMR has been highly ranked at the global and national level in the Government Sector Institutions. I am sure CBMR will work with a renewed zeal to further improve the rankings.

During the reporting period, the Centre has progressed well at the academic front. A total of 72 research papers were published in journals of international repute with an average impact factor of 4.27. Four Indian patents and one international patent were filed. 12 new extramural projects were sanctioned, with a total extramural funding of ≈ Rs. 558.00 Lakhs. Ten PhD degrees were awarded at CBMR.

CBMR also participated in societal programmes in which school students visited CBMR to see first-hand the research being undertaken at the Centre. Also, faculty and students of the Centre participated in the road safety programmes as well as awareness programmes against COVID.

CBMR has been successfully working towards establishing its role as a leading R&D Organization of the country that plays an important role in addressing the societal needs and better patient care. I would like to assure that the hard-work put in by the faculty and staff of CBMR will continue to position this Centre at a global level in niche areas of biology and chemistry. I am sure that the CBMR, while addressing the needs of the State and National mission programmes, will grow further in line with its vision and mission.

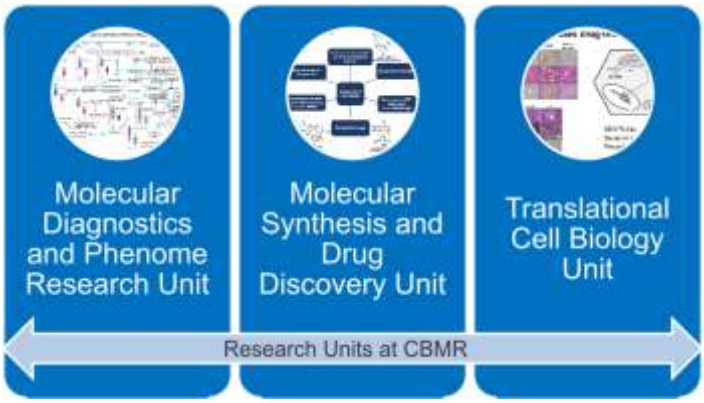
I should like to express my gratitude to the Chairperson and Members of the Governing Council, CBMR for their visionary guidance and valuable support. I should also like to thank the Department of Medical Education, Government of Uttar Pradesh for extending their full cooperation and financial support for smooth functioning of the Centre. I am grateful to Chairman and Members of the Scientific Advisory Committee (SAC) for their constructive and critical comments in shaping the scientific programme of the Centre. I am indeed grateful to the Hon'ble Cabinet Minister and Hon'ble State Minister, Department of Medical Education, Government of Uttar Pradesh, for their invaluable guidance and support. I wish to place on record my sincere gratitude to the Hon'ble Chief Minister, Uttar Pradesh for his constant support and encouragement to CBMR.

**(Alok Dhawan)**

# Centre of BioMedical Research

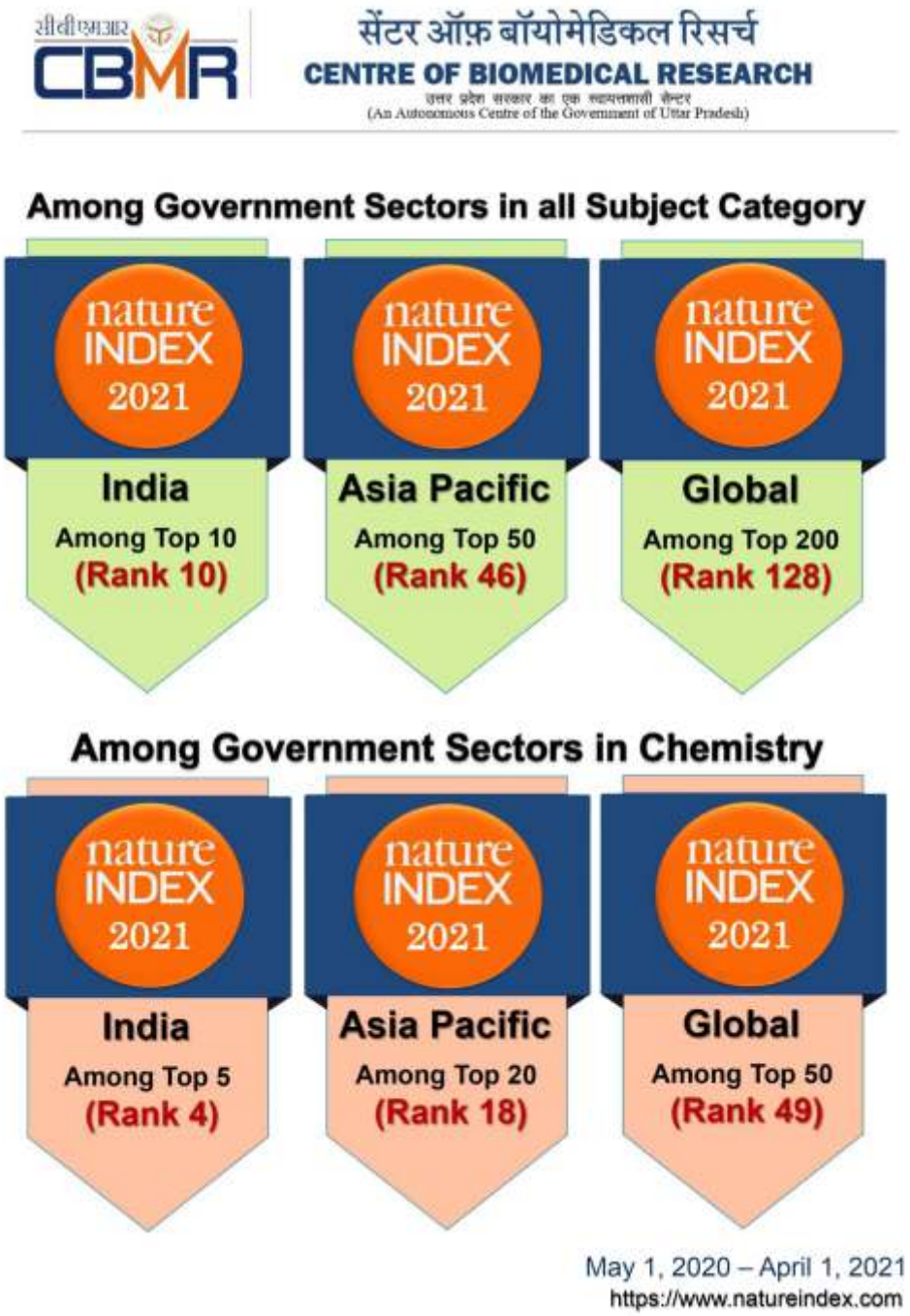
CBMR is an autonomous Centre of the Government of Uttar Pradesh under the Department of Medical Education. It was established as “Centre of Biomedical Magnetic Resonance”. To broaden the scope of the Centre, the Government of Uttar Pradesh in 2013 rechristened it as “Centre of BioMedical Research". CBMR is a uniquely positioned centre in the country and perhaps one of the few in the world which is solely dedicated to identification of biomarkers and validating them both clinically and functionally. CBMR is involved in basic, applied and translational aspects of biology and chemistry. The state-of-the-art equipment at CBMR include NMR (400, 600, 800 MHz – Solution and Solid State), 3T-fMRI, as well as sophisticated analytical facility which provide a platform for academician, industry and entrepreneurs to ideate, collaborate and co-create with the following vision and mission.

- To undertake, aid, promote, develop, guide and coordinate basic, clinical and translational research.
- The mission of CBMR is to establish an enabling ecosystem for cutting edge interdisciplinary research and entrepreneurship leading to better patient care.

# Nature Index-2021

Center of BioMedical Research has been recognized globally by Nature Index-2021 (from May 01, 2020 to April 01, 2021) as per the rankings given below:



Professor Alok Dhawan, Director, CBMR with Hon'ble Governor, Uttar Pradesh

Professor Alok Dhawan, Director, CBMR with Hon'ble Deputy Chief Minister, Uttar Pradesh

Professor Alok Dhawan, Director, CBMR with Hon'ble Minister, Department of Medical Education, Government of Uttar Pradesh

Professor Alok Dhawan, Director, CBMR with President CBMR & Chief Secretary, Government of Uttar Pradesh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**Governor of Uttar Pradesh**
20 July

उत्तर प्रदेश की राज्यपाल श्रीमती आनंदीबेन पटेल से आज राजभवन में जैव चिकित्सा अनुसंधान केन्द्र, लखनऊ के निदेशक डॉ० आलोक धावन ने शिष्टाचार भेंट की और संस्थान द्वारा किये जा रहे नवीनतम शोध कार्यों से संबंधित एक विवरणिका दी।
राज्यपाल जी ने अनुसंधान केन्द्र द्वारा टी०बी०, तिवर तथा हड्डियों की जांच के साथ ही कोविड-19 से उत्पन्न अनेक बीमारियों पर किये जा रहे शोध कार्यों की प्रशंसा की। उन्होंने कहा कि जैव चिकित्सा अनुसंधान केन्द्र द्वारा चिकित्सा एवं अनुसंधान के क्षेत्र में जो अनुकरणीय कार्य किया जा रहा है, उसका लाभ गम्भीर रोग से ग्रस्त गरीब लोगों को मिलने से उनकी सहायता होगी।

See translation

15

Like Comment Share

**आनंदीबेन पटेल**
राज्यपाल, उत्तर प्रदेश

सत्यमेव जयते

राज भवन
लखनऊ - 226 027

## सन्देश

मुझे यह जानकर अत्यन्त प्रसन्नता हुई कि सेंटर ऑफ बायोमेडिकल रिसर्च (सी0बी0एम0आर0) उत्तर प्रदेश सरकार द्वारा चिकित्सा शिक्षा विभाग के अन्तर्गत स्थापित एक स्वायत्तशासी सेंटर है, जो कि भारत में लगभग 15 वर्षों से जैव चिकित्सा के क्षेत्र में अनुसंधान करने वाला एक संस्थान है।

यह हर्ष का विषय है कि संस्थान को नेचर इंडेक्स द्वारा विश्व स्तर पर सराहनीय स्थान प्रदान किया गया है। मुझे पूर्ण विश्वास है कि संस्थान इसी प्रकार अपने क्षेत्र में बहुमूल्य योगदान से अपनी गुणवत्ता का संवर्द्धन करता रहेगा।

मैं सेंटर ऑफ बायोमेडिकल रिसर्च को अपनी हार्दिक शुभकामनाएँ प्रेषित करती हूँ।

आनंदीबेन

( आनंदीबेन पटेल )

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Acharya Devvrat
Governor, Gujarat
Gandhinagar-382021

सत्यमेव जयते

आचार्य देवव्रत
राज्यपाल, गुजरात
गांधीनगर-३८२०२१

# संदेश

यह अत्यंत हर्ष का विषय है कि उत्तर प्रदेश सरकार का एक स्वायत्तशासी सेन्टर के रूप में सेन्टर ऑफ बायोमेडिकल रिसर्च सी. बी. एम. आर. ने जैव चिकित्सा के क्षेत्र में अपने अनुसंधान कार्य से देश और विदेशों में भी ख्याति प्राप्त की है। यह सेन्टर चिकित्सा क्षेत्र में महत्त्वपूर्ण शोध एवं अनुसंधान संबंधी कार्यों में अहम भूमिका निभा रहा है।

इस सेन्टर के सफलतम कार्यों की नेचर इंडेक्स द्वारा वैश्विक स्तर पर सराहना की गई है, जिसके अंतर्गत 1 मई, 2020 से 1 अप्रैल, 2021 तक के समय में समस्त विषय श्रेणी में सरकारी क्षेत्रों के अंतर्गत समग्र देश में 10वां स्थान, एशिया प्रशांत विस्तार में 46वां और विश्व में 128वां स्थान एवं रसायन विज्ञान में देश में चौथा, एशिया प्रशांत विस्तार में 18वां और विश्व में 49वां स्थान मिला है, जो सचमुच गौरव की बात है। इस सेन्टर की उत्तरोत्तर प्रगति की कामना करता हूँ और हार्दिक शुभकामनाएँ प्रेषित करता हूँ।

(आचार्य देवव्रत)

कलराज मिश्र
राज्यपाल, राजस्थान

सत्यमेव जयते

Kalraj Mishra
Governor, Rajasthan

# संदेश

मुझे यह जानकर प्रसन्नता हुई है कि सेंटर ऑफ बॉयोमेडिकल रिसर्च (सी. बी.एम.आर.) लखनऊ, को नेचर इंडेक्स द्वारा विश्व स्तर पर रामसा विषय श्रेणी में सरकारी क्षेत्र के अन्तर्गत शीर्ष 10वें और रसायन विज्ञान में शीर्ष चौथा स्थान प्राप्त हुआ है। यूनाईटेड किंगडम से प्रकाशित नेचर पत्रिका द्वारा आपके इस संस्थान को प्रदत्त इस उपलब्धि के लिए मेरी हार्दिक बधाई स्वीकारें।

जैव चिकित्सा वर्तमान समय में रोगोपचार की बेहद महत्वपूर्ण पद्धति है। जटिल रोगों की पहचान एवं निदान के परीक्षण के साथ ही जीन थेरेपी से इसके अंतर्गत असाध्य रोगों के उपचार के क्रांतिकारी परिणाम प्राप्त हुए हैं। मुझे इस बात की प्रसन्नता है कि लखनऊ स्थित आपका संस्थान जैव चिकित्सा के क्षेत्र में देशभर में अनुसंधान करने वाला भारत का अग्रणी संस्थान है। चिकित्सकों के लिए मरीजों के जटिल रोगों की पहचान एवं निदान के लिए परीक्षण करने तथा इस संबंध में मौलिक शोध करने में संस्थान के रामसा सदस्यों की भूमिका की मैं सराहना करता हूं।

विश्वास है, आपका संस्थान जैव चिकित्सा अनुसंधान क्षेत्र में इसी तरह भविष्य में भी विश्वभर में शीर्ष स्थान बनाता रहेगा।

मेरी हार्दिक शुभकामना है।

(कलराज मिश्र)

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## शुभकामना संदेश

मुझे यह जानकर अत्यन्त प्रसन्नता हुयी कि उत्तर प्रदेश सरकारद्वारा चिकित्सा शिक्षा विभाग के अन्तर्गत स्थापित स्वायत्तशासी "सेन्टर ऑफ बायोमेडिकल रिसर्च (सी0बी0एम0आर0), लखनऊ कोनेचर इंडेक्स द्वारा विश्वपटल पर प्रदान की गई रैंकिंग में प्रशंसनीय स्थान प्राप्त किया है.

मेरी जानकारी में सेन्टर लगभग 15 वर्षोंसे जैवचिकित्सा के क्षेत्र में अनुसंधान करनेवाला भारत का एक अग्रणी संस्थान है. यह सेन्टर अत्यन्त आधुनिक उपकरणों से सुशोभित है. सेन्टर उच्च स्तरीय चिकित्सा / शोध संस्थानों में आनेवाले रोगियों के जटिल रोगों के परीक्षण एवं उसके निदान के क्षेत्र में इन उपकरणों के माध्यम से विभिन्न अतिविशिष्ट विधाओंके चिकित्सकों के साथ मिलकर महत्वपूर्ण शोध एवं अनुसंधान सम्बन्धी कार्यों में अहम् भूमिका निभा रहा है.

मुझे विश्वास है कि सी0बी0एम0आर0 भविष्य में इस से भी बेहतर कार्य करेगा तथा इसी प्रकार उत्तर प्रदेश का नाम राष्ट्रीय एवं अन्तर्राष्ट्रीय स्तर पर गौरवान्वित करता रहेगा.

मैं सी0बी0एम0आर0 को हृदय से बधाई एवं शुभकामनाएं देता हूँ.

(राम नाईक)

निवास : बी 503 लक्षचंडी अपार्टमेंट्स, कृष्ण वाटिका मार्ग, गोकुलधाम, गोरेगाव पूर्व, मुंबई 400 063 दूरभाष: 022-28413399

राजनाथ सिंह
RAJNATH SINGH

सत्यमेव जयते

रक्षा मंत्री
भारत
DEFENCE MINISTER
INDIA

## संदेश

मुझे यह जानकर हार्दिक प्रसन्नता हुई है कि **चिकित्सा शिक्षा विभाग** के अन्तर्गत स्थापित स्वायत्तशासी **सेन्टर फॉर बायोमेडिकल रिसर्च (सी.बी.एम.आर.), लखनऊ, उत्तर प्रदेश** को **नेचर इंडेक्स** द्वारा विश्व पटल पर शीर्ष संस्थानों की सूची में एक सराहनीय रैंकिंग प्रदान की गई है।

मैं सी.बी.एम.आर. परिवार से जुड़े सभी सदस्यों को इसके लिए हार्दिक बधाई देता हूं तथा सी.बी.एम.आर. को अपनी शुभकामनाएं प्रेषित करता हूं कि वह भविष्य में भी इसी प्रकार सफलता के नए कीर्तिमान स्थापित करता रहे।

शुभकामनाओं सहित।

(राजनाथ सिंह)

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संख्या-

योगी आदित्यनाथ

मुख्य मंत्री
उत्तर प्रदेश

लोक भवन,
लखनऊ-226001

## संदेश

मुझे यह जानकर अत्यन्त प्रसन्नता की अनुभूति हो रही है कि उत्तर प्रदेश सरकार द्वारा चिकित्सा शिक्षा विभाग के अन्तर्गत स्थापित स्वायत्तशासी सेण्टर ऑफ बायोमेडिकल रिसर्च (सी0बी0एम0आर0) लगभग 15 वर्षों से जैव चिकित्सा के क्षेत्र में अनुसंधान करने वाला भारत का एक अग्रणी संस्थान है।

सी0बी0एम0आर0 द्वारा नेचर इण्डेक्स (Nature Index-2021) की वैश्विक रैंकिंग में उल्लेखनीय स्थान प्राप्त किया जाना अत्यन्त सराहनीय है। मुझे आशा है कि यह संस्थान भविष्य में भी इसी प्रकार उच्चस्तरीय शोध कार्यों में संलग्न रहकर प्रदेश के गौरव में वृद्धि करता रहेगा।

सेण्टर ऑफ बायोमेडिकल रिसर्च के उज्ज्वल भविष्य हेतु मेरी हार्दिक शुभकामनाएं।

( योगी आदित्यनाथ )

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**डॉ0 दिनेश शर्मा**

उप मुख्यमंत्री
उत्तर प्रदेश

99-100, विधान भवन,
लखनऊ

## सन्देश

मुझे यह जानकर अत्यन्त प्रसन्नता हो रही है कि सेन्टर ऑफ बायोमेडिकल रिसर्च, उ0प्र0 लखनऊ को नेचर इंडेक्स–2021 में समस्त विषय श्रेणी में सरकारी क्षेत्रों के अन्तर्गत विश्व के शीर्ष 200 संस्थानों में से 128वाँ स्थान, एशिया प्रशान्त के 50 शीर्ष संस्थानों में से 46वाँ स्थान एवं भारत के 10 शीर्ष संस्थानों में से 10वाँ स्थान प्राप्त करने के साथ ही साथ रसायन विज्ञान में सरकारी क्षेत्रों के अन्तर्गत विश्व के शीर्ष 50 संस्थानों में से 49वाँ स्थान, एशिया प्रशान्त के 20 शीर्ष संस्थानों में से 18वाँ स्थान एवं भारत के 05 शीर्ष संस्थानों में से तीसरा स्थान प्राप्त करना अत्यन्त सराहनीय है। इस हेतु आप तथा आपकी पूरी टीम बधाई के पात्र हैं।

इंडेक्स नेचर की कल्पना नेचर्य रिसर्च द्वारा की गयी थी। नेचर इंडेक्स 82 उच्च गुणवत्ता वाले विज्ञान पत्रिकाओं के स्वतंत्र रूप से चयनित समूह में प्रकाशित शोध पत्रों के आधार पर बनाया गया एक डेटाबेस है, जिसमें 10,000 से अधिक संस्थान सूचीबद्ध है। सेन्टर ऑफ बायोमेडिकल रिसर्च, उ0प्र0 सरकार के चिकित्सा शिक्षा विभाग द्वारा स्थापित एक स्वयत्तशासी सेन्टर है, जो लगभग 15 वर्षों से जैव चिकित्सा के क्षेत्र में अनुसंधान करने वाला भारत का एक अग्रणी संस्थान है। सेन्टर द्वारा शीघ्र ही उ0प्र0 स्टार्ट–अप नीति 2020 के तहत नवाचार तथा उद्यमशीलता के लिए इन्क्यूबेटर की स्थापना की जा रही है।

मुझे आशा ही नहीं बल्कि पूर्ण विश्वास है कि सेन्टर ऑफ बायोमेडिकल रिसर्च, उ0प्र0, लखनऊ आगामी वर्षों में भी इसी प्रकार सफलता के नये कीर्तिमान स्थापित करता रहेगा।

(डॉ. दिनेश शर्मा)

सुरेश कुमार खन्ना
मंत्री
वित्त, संसदीय कार्य एवं
चिकित्सा शिक्षा विभाग

सं0 76 पं0वि0सं0का0चि0शि0/शुभकामना सदेश/2021

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# सन्देश

उत्तर प्रदेश सरकार द्वारा चिकित्सा शिक्षा विभाग के अन्तर्गत स्थापित स्वायत्तशासी सेन्टर ऑफ बायोमेडिकल रिसर्च (सी0बी0एम0आर0), लखनऊ को नेचर इंडेक्स द्वारा विश्व पटल पर प्रदान की गई रैंकिंग में आपके संस्थान ने सराहनीय कार्य किया है।

आशान्वित हूँ कि आपके कुशल नेतृत्व में आपका संस्थान भविष्य में इससे भी बेहतर प्रगति की ओर अग्रसर होगा।

(सुरेश कुमार खन्ना)

आशुतोष टण्डन "गोपाल जी"
मन्त्री
नगर विकास, शहरी समग्र विकास,
नगरीय रोजगार एवं गरीबी उन्मूलन विभाग

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सी.एच. : 2213251
कक्ष संख्या 59–59ए, मुख्य भवन
विधान भवन, लखनऊ

## संदेश

मुझे यह जानकर प्रसन्नता हो रही है कि सेन्टर ऑफ बायोमेडिकल रिसर्च (सी0बी0एम0आर0), लखनऊ को नेचर इंडेक्स द्वारा विश्व पटल पर प्रदान की गयी रैंकिग में राष्ट्रीय एवं अन्तर्राष्ट्रीय स्तर पर सराहनीय स्थान प्राप्त हुआ है।

सेन्टर ऑफ बायोमेडिकल रिसर्च लगभग 15 वर्षो से शोध एवं अनुसंधान सम्बन्धी कार्यो में अहम भूमिका निभा रहा है। जैव चिकित्सा के क्षेत्र में अनुसंधान करने वाला भारत का यह एक अग्रणी संस्थान है। मुझे आशा है कि सेन्टर ऑफ बायोमेडिकल रिसर्च (सी0बी0एम0आर0) इसी प्रकार उत्कृष्ट शोध करता रहेगा, जिसके माध्यम से प्रत्यक्ष एवं परोक्ष रूप से आम जनता लाभान्वित होती रहेगी।

सी0बी0एम0आर0 के समस्त कर्मियों एवं शोध छात्र/छात्राओं को मेरी हार्दिक शुभकामनाएं।

(आशुतोष टण्डन)

सत्यमेव जयते

SANJAY SETH
MEMBER OF PARLIAMENT
(RAJYA SABHA)

## शुभकामना संदेश

मुझे यह जानकर बड़ी प्रशन्नता हो रही है कि उत्तर प्रदेश सरकार द्वारा चिकित्सा शिक्षा विभाग के अंतर्गत स्थापित स्वायतशासी "सेन्टर ऑफ बायोमेडिकल रिसर्च" (सी0बी0एम0आर0), लखनऊ को नेचर इंडेक्स द्वारा विश्व पटल पर प्रदान की गई रैंकिग में अग्रणीय स्थान प्राप्त किया है।

जैसा कि ज्ञात हुआ कि सेन्टर लगभग 15 वर्षों से जैव चिकित्सा के क्षेत्र में अनुसंधान करने वाला भारत का एक अग्रणी संस्थान है। सेन्टर द्वारा उच्च स्तरीय चिकित्सा / शोध संस्थानों में आने वाले रोगियों के जटिल रोगों के परीक्षण एवं उसके निदान के क्षेत्र में अत्यंत आधुनिक उपकरणों के माध्यम से विभिन्न अतिविशिष्ट विधाओं के चिकित्सकों के साथ मिल कर महत्वपूर्ण शोध एवं अनुसंधान संबधी कार्यों में अहम भूमिका निभा रहा है।

मैं आशान्वित हूँ कि सी0बी0एम0आर0 अपने शोध कार्यों के माध्यम से इसी प्रकार प्रदेश का नाम राष्ट्रीय एवं अंतराष्ट्रीय स्तर पर गौरवान्वित करता रहेगा।

इन उत्कृष्ट कार्यों के लिये मैं सी0बी0एम0आर0 को हृदय से बधाई एवं शुभकामानाएं देता हूँ।

(संजय सेठ)

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**Lucknow Resi.** : 8/1, Vikramaditya Marg, Lucknow - 226 001 (Uttar Pradesh)
Ph.: 0522-4030444 / 2239995, Mobile : 7705012838

**डा.नीरज बोरा**
एम.बी.बी.एस., एम.बी.ए.
विधायक
लखनऊ उत्तर विधान सभा
सदस्य- स्थानीय निकायों की लेखा परीक्षा प्रतिवेदनों
की जाँच सम्बन्धी समिति विधानसभा, उ0प्र0

सदस्य विधान सभा उत्तर प्रदेश

ख-6 № 712363

## शुभकामना सन्देश

अति गर्व का विषय है कि "चिकित्सा शिक्षा विभाग के अन्तर्गत", स्थापित स्वायत्तशासी **सेन्टर फॉर बायोमेडिकल रिसर्च (सी0बी0एम0आर0), लखनऊ उत्तर प्रदेश** जैव चिकित्सा के क्षेत्र में अग्रणीय योगदान दे रहा है। इस संस्थान के द्वारा किये जा रहे अनुसंधान से मरीजों को लाभ पहुंचा है। इस लिए आप का संस्थान बधाई का पात्र है। हाल ही में **नेचर इंडेक्स** द्वारा विश्व पटल पर शीर्ष संस्थानों की सूची में सी0बी0एम0आर0 को सराहनीय रैंकिंग प्रदान की गई है।

मैं संस्थान **सेन्टर फॉर बायोमेडिकल रिसर्च (सी0बी0एम0आर0), लखनऊ उत्तर प्रदेश** से जुड़े समस्त सदस्यों को उनके जन कल्याणकारी कार्यों के लिए हार्दिक बधाई तथा **नेचर इंडेक्स** में प्राप्त हुई रैंकिंग हेतु शुभकामनाएं प्रेषित करता हूं।

शुभकामनाओं सहित।

(डा. नीरज बोरा)

**प्रधान कार्यालय : सेवा अस्पताल परिसर, सेवा नगर, सीतापुर रोड, लखनऊ-226201**
**कैम्प कार्यालय : 82-83, सेक्टर-डी, प्रियदर्शिनी कालोनी, सीतापुर रोड, लखनऊ-226020**
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I 4/01/2021

डॉ. राजीव कुमार
उपाध्यक्ष
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सत्यमेव जयते
Azadi Ka Amrit Mahotsav

भारत सरकार
नीति आयोग, संसद मार्ग
नई दिल्ली - 110 001
Government of India
NATIONAL INSTITUTION FOR TRANSFORMING INDIA
NITI Aayog, Parliament Street,
New Delhi - 110 001

I am delighted to receive your letter dated the 01st September, 2021, outlining the achievements of the Centre of Biomedical Research (CBMR), Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow.

2. The CBMR's dedicated study of biomarkers is noteworthy. The recent pandemic has underlined the critical importance of rapidly identifying and validating biomarkers. I also find the CBMR's work in molecular synthesis and drug discovery to be very promising. Therefore, I greatly appreciate the CBMR's performance in the Nature Index 2020-2021, and make a special note of its leading performance in the Asia Pacific Region (top 50 among Government sectors in All Subjects) and Globally (top 50 among Government sectors in Chemistry).

3. I will like to take this opportunity to encourage the innovative minds in the CBMR to explore and expand partnerships with other academic and research institutes to accelerate multi-disciplinary research. I will also encourage you to accelerate the lab-to-market processes to ensure that the research output can be transformed into a solution that reaches the people. By doing this, I am certain that the CBMR can bag even higher achievements.

4. I thank you for writing to me and encourage you to keep me apprised of any issues that the NITI Aayog can assist you with to support your noteworthy 'Prayas'.

Best regards,

Yours sincerely,

Rkumar

(Rajiv Kumar)

स्वच्छ भारत
एक कदम स्वच्छता की ओर

अमिताभ कांत
Amitabh Kant
मुख्य कार्यकारी अधिकारी
Chief Executive Officer

भारत सरकार
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## Message

It gives me immense pleasure to extend my Congratulations to Centre of Bio-Medical Research (CBMR) for its commendable performance in 'Nature Index 2021'. I appreciate the efforts of CBMR in achieving its vision of supporting research for prevention, early disease diagnosis and treatment monitoring through identification and validation of biomarkers.

Novel research in biomedical sector must be promoted to tackle the existing disease burden and ensure emerging technologies like precision medicine become accessible and affordable for all.

I applaud the contribution of the faculty, staff members, scientists, research scholars and students of CBMR in ensuring that top-quality research is carried out in the country. I encourage you to publish your research extensively and ensure that novel ideas reach the market so that evidence-based, reliable treatment can be provided to our citizens and the world. I am sure that CBMR will reach greater heights in the coming future.

(Amitabh Kant)

स्वच्छ भारत
एक कदम स्वच्छता की ओर

डॉ. वी.के. सारस्वत
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सत्यमेव जयते

भारत सरकार
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नई दिल्ली - 110 001
Government of India
National Institution for Transforming India
NITI Aayog, Parliament Street,
New Delhi - 110 001

**MESSAGE**

I am happy to learn that the Centre of Biomedical Research (CBMR), under the Department of Medical Education, Government of Uttar Pradesh, set up in 1999 to establish a close link among the basic and the clinical scientists and to generate appropriate human resource to fully exploit the potentials in Magnetic Resonance, is carrying out pioneering research in interdisciplinary aspects of Magnetic Resonance and developing the appropriate human resource at the national level.

It is very heartening to note that CBMR's recently published "Nature Index 2021", a database of author affiliation information, has made to the top 10 in both "Government Sector All Subject Category" and "Government Sector in Chemistry" in India and made it to the top-50 in the Global ranking in "Government Sector Chemistry". The Nature Index also provides real time proxy of high quality research output and collaboration at the institutional, national and regional levels.

I congratulate Prof. Alok Dhawan and other office-bearers and officers of CBMR on this excellent achievement and wish CBMR all success in all their future endeavours.

(DR. V.K. SARASWAT)

New Delhi

स्वच्छ भारत
एक कदम स्वच्छता की ओर

सत्यमेव जयते

डॉ. रेणु स्वरूप
DR. RENU SWARUP

सचिव
भारत सरकार
विज्ञान और प्रौद्योगिकी मंत्रालय
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SECRETARY
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MINISTRY OF SCIENCE & TECHNOLOGY
DEPARTMENT OF BIOTECHNOLOGY
Block-2, 7th Floor, C.G.O. Complex
Lodhi Road, New Delhi-110003

D.O. No. SBT/97/2021

I am happy to know that the Centre of Bio-Medical Research (CBMR), an autonomous Centre of the Government of Uttar Pradesh has been ranked in the Government Sector at a global and national level in the newly published rankings of Nature Index 2021.

DBT has been supporting the Centre through extramural projects and has witnessed its growth over time, and a unique Centre dedicated to the identification of biomarkers and validating them both clinically and functionally.

The ranking obtained is a proof of the quality research work being carried out at CBMR.

Congratulations to team CBMR, your efforts should now be to scale up the ranking in terms of not just national but also global recognition.

Wishing you all a bright future ahead.

Yours sincerely,

(Renu Swarup)

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सत्यमेव जयते

डॉ. शेखर चिं. मांडे
एफएनए, एफएएसी, एफएनएएससी
सचिव
वैज्ञानिक और औद्योगिक अनुसंधान विभाग तथा
महानिदेशक
Dr. Shekhar C. Mande
FNA, FASc, FNASc
Secretary
Department of Scientific & Industrial Research and
Director General

भारत सरकार
विज्ञान और प्रौद्योगिकी मंत्रालय
वैज्ञानिक तथा औद्योगिक अनुसंधान परिषद
वैज्ञानिक और औद्योगिक अनुसंधान विभाग
Government of India
Ministry of Science and Technology
Council of Scientific & Industrial Research
Department of Scientific & Industrial Research

NO.DG/PS/CSIR/2021/64

I note with immense happiness that the Centre of Biomedical Research is among the Top 10 Government Sector Institute in the prestigious Nature Index. It is also heartening to note that the centre is among the top five government Sector Institutions in chemistry.

These rankings are an indicator of the excellent research being carried out in the Centre for Biomedical Research. I congratulate you on this achievement and wish all the faculty and staff of CBR.

I am sure that the Centre will scale newer heights under your able leadership. My best wishes.

With best regards,

Your Sincerely,

(Shekhar C. Mande)

Anusandhan Bhawan, 2, Rafi Marg, New Delhi-110001
Tel. : 23710472, 23717053, Fax : (91-11) 23710618, E-mail : secy-dsir@gov.in, dgcsir@csir.res.in and dg@csir.res.in, Website : www.csir.res.in

के. एन. व्यास
**K. N. Vyas**

सत्यमेव जयते
भारत सरकार
**Government of India**

अध्यक्ष, परमाणु ऊर्जा आयोग
व
सचिव, परमाणु ऊर्जा विभाग
**Chairman, Atomic Energy Commission**
**&**
**Secretary, Department of Atomic Energy**

No. 133/2021

This has reference to your letter No. CBMR/ESTAB/NI/823/2021/2050 dated August 5, 2021 regarding listing of CBMR in Nature Index global ranking.

We are aware of the continuing contributions of your Institute for biomedical research especially in the area of molecular diagnosis for identification of biomarkers and their validation clinically and functionally.

Please accept my heartiest congratulation for the excellent scientific contributions you and your faculty members at CBMR have made during May 1, 2020 to April 1, 2021 which positioned you into one of the highest Nature Index 2020-21 rankings amongst the Government Sector in All Subjects Category as well as in Chemistry Category.

The achievement would not have been possible without an able leadership and great team work.

Please convey my heartiest congratulations to all your colleagues of CBMR and I wish them many more successes to achieve greater heights in future.

Thanking you and with best regards,

Yours sincerely,

(K.N. Vyas)

अणुशक्तिभवन, छत्रपति शिवाजी महाराज मार्ग, मुंबई - 400 001, भारत • Anushakti Bhavan, Chhatrapati Shivaji Maharaj Marg, Mumbai - 400 001, India
दूरभाष/Phone:+(91) (22) 2202 2543 • फैक्स/Fax: +(91) (22) 2204 9476 / 2284 3888
ई-मेल/E-mail: chairman@dae.gov.in

सत्यमेव जयते

**प्रोफेसर (डा.) बलराम भार्गव,** पद्म श्री
एम.डी., डी.एम., एफ.आर.सी.पी. (जी.), एफ.आर.सी.पी. (ई.), एफ.ए.सी.सी.,
एफ.ए.एच.ए., एफ.ए.एम.एस., एफ.एन.ए.एस., एफ.एस.सी., एफ.एन.ए., डी.एस.सी.
**सचिव, भारत सरकार**
स्वास्थ्य अनुसंधान विभाग
स्वास्थ्य एवं परिवार कल्याण मंत्रालय एवं
**महानिदेशक, आई सी एम आर**

**Prof. (Dr.) Balram Bhargava,** Padma Shri
MD, DM, FRCP (Glasg.), FRCP (Edin.),
FACC, FAHA, FAMS, FNASc, FASc, FNA, DSc
**Secretary to the Government of India**
Department of Health Research
Ministry of Health & Family Welfare &
**Director-General, ICMR**

**भारतीय आयुर्विज्ञान अनुसंधान परिषद**
स्वास्थ्य अनुसंधान विभाग
स्वास्थ्य एवं परिवार कल्याण मंत्रालय
भारत सरकार
वी. रामलिंगस्वामी भवन, अंसारी नगर
नई दिल्ली - 110 029

**Indian Council of Medical Research**
Department of Health Research
Ministry of Health & Family Welfare
Government of India
V. Ramalingaswami Bhawan, Ansari Nagar
New Delhi - 110 029

## MESSAGE

It is heartening to see that the Centre of Bio-Medical Research (CBMR) which is an autonomous Centre of the Government of Uttar Pradesh has obtained excellent ranking in the Government Sector both in the country as well as globally in the recently published Nature Index ranking 2021.

This is yet another outcome of the top quality research being pursued at CBMR.

I would like to congratulate to the entire team of CBMR on this hard-earned achievement and wish you all great success in your future endeavors as well.

Balram Bhargava

( Balram Bhargava )

Tele.: 26588204, 26589620, Fax (Off.) : 91-11-26588662, E-mail: secy-dg@icmr.gov.in

सत्यमेव जयते
प्रो. आशुतोष शर्मा
Prof. Ashutosh Sharma

सचिव
भारत सरकार
विज्ञान और प्रौद्योगिकी मंत्रालय
विज्ञान और प्रौद्योगिकी विभाग
**Secretary**
**Government of India**
Ministry of Science and Technology
**Department of Science and Technology**

## MESSAGE

It is indeed a matter of delight that the Centre of Bio-Medical Research (CBMR) which is an autonomous Centre of the Government of Uttar Pradesh has received international and national ranking in the recently published list of Nature Index 2021 in the Government Sector. Department of Science and Technology (DST) has been supporting the Centre through projects and has seen it grow from strength to strength over the years. CBMR is a unique Centre of the country solely dedicated to bio-medical research leading to better patient care. The ranking reflects the quality of fundamental research pursued at CBMR. Needless to say that the translation research being pursued at CBMR, is equally relevant and important for the country. Working at the interface of biology and chemistry, I am sure CBMR will reach greater heights. I congratulate the faculty and students of CBMR for this outstanding achievement and wish you all a bright future ahead.

(Ashutosh Sharma)

**Technology Bhavan, New Mehrauli Road, New Delhi - 110016**
**Tel: 00 91 11 26511439 / 26510068 | Fax: 00 91 11 26863847 | e-mail: dstsec@nic.in | website: www.dst.gov.in**

भारतीय राष्ट्रीय विज्ञान अकादमी
बहादुर शाह ज़फ़र मार्ग, नई दिल्ली–110002
INDIAN NATIONAL SCIENCE ACADEMY
Bahadur Shah Zafar Marg, New Delhi-110002

प्रोफेसर चंद्रिमा शाहा
अध्यक्ष
Prof. Chandrima Shaha
President

No.Pr/INSA2021

I am pleased to see the well deserved success achieved by CBMR by getting listed in the Nature Index (2020-2021) Global ranking . This is a great achievement. My heartiest congratulations to you and the entire Faculty of CBMR who have worked hard to earn this position.

CBMR is a unique institution which is solely dedicated to identification of biomarkers and validating them both clinically and functionally. I am sure under your guidance, the CBMR will reach to newer heights.

With warm regards,

Yours sincerely,

Chandrima Shaha

**(Chandrima Shaha)**

❑ टेलीफ़ोन / Tel. : +91-11-2323 5865 (Dir), 2323 5153, 2322 1931 - 2322 1950 ❑ (ई. पी. ए. बी. एक्स./EPABX)
❑ फैक्स / Fax : +91-11-2323 1095, 23235648 ❑ ई-मेल / Email : president@insa.nic.in, esoffice@insa.nic.in

डा० संजीव मिश्रा
Dr. Sanjeev Misra
MS, MCh, FRCS (Eng.), FRCS (Glasgow), FICS, FACS (USA), FAMS, FNASc
Director & CEO
Prof. of Surgical Oncology

अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
All India Institute of Medical Sciences, Jodhpur-342005, Rajasthan, India
Phone : 0291-2012993
E-mail : director@aiimsjodhpur.edu.in
misralko@gmail.com

D.O. No. 273

**MESSAGE**

It gives me great pleasure to know that Centre of Biomedical Research (CBMR) is contributing towards new knowledge in the area of biomedical science and has been ranked very highly by Nature Index ranking published in 2021. It is heartening to know that CBMR has continued its journey of excellence by conducting world class research solely dedicated for the benefit of common man including patients. I congratulate the staff, students and faculty of CBMR for the exemplary global ranking in Nature Index.

I look forward to many more accomplishments of CBMR in the future.

**(Dr. Sanjeev Misra)**
Director

Basni, Phase-II, Jodhpur Rajasthan-342005. Phone : 0291-2740535 Fax: 0291-2740531 Website: www.aiimsjodhpur.edu.in

iCreate
International Centre for Entrepreneurship and Technology

It is with great pleasure that I note that CBMR has received both national and international rankings in Nature Index 2021 for its outstanding fundamental research. This further strengthens the resolve of the faculty and all of us in the Governing Council to support such fundamental science being pursued at CBMR. Further, I am happy note the translational research being done at CBMR which not only helps the patients at the local hospitals but has tremendous potential for commercialisation.

I congratulate the faculty of CBMR for achieving this feat and am sure under your dynamic leadership CBMR will reach greater heights in the years to come.

Kind regards,

Anupam Jalote
CEO iCreate

**An initiative of Gujarat Foundation for Entrepreneurial Excellence**

**Regd. Off.:** First Floor, GMDC Building, 132 ft. Ring Road, Vastrapur, Ahmedabad 380052, India.
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**अवनीश कुमार अवस्थी**
आई.ए.एस.
अपर मुख्य सचिव

फोन: 0522-2289291, 0522-2226091,
0522-2226092
ई–मेल: pshomelko@gmail.com
अर्द्धशा०पत्र सं०2।3ने/ए.सी.एस. /2021
गृह, गोपन, वीजा, पासपोर्ट, सतर्कता, कारागार
एवं धर्मार्थ कार्य विभाग
लोक भवन, उत्तर प्रदेश शासन।

## सन्देश

मुझे यह जानकर अत्यंत प्रसन्नता हुई कि सेन्टर ऑफ बायोमेडिकल रिसर्च (सी0बी0एम0आर0), लखनऊ नेचर इंडेक्स द्वारा विश्व पटल पर प्रदान की गई रैंकिग में अग्रणीय स्थान प्राप्त किया है। यह उत्तर प्रदेश सरकार द्वारा चिकित्सा शिक्षा विभाग के अन्तर्गत स्थापित एक स्वायत्तशासी सेन्टर है।

लगभग 15 वर्षों से जैव चिकित्सा के क्षेत्र में अनुसंधान करने वाला यह सेन्टर भारत का एक अग्रणी संस्थान है। यह सेन्टर अत्यन्त आधुनिक उपकरणों के माध्यम से महत्वपूर्ण शोध एवं अनुसंधान सम्बन्धी कार्यों में अहम भूमिका निभा रहा है।

मुझे आशा ही नही अपितु पूर्ण विश्वास है कि यह सेन्टर भविष्य में इसी तरह बेहतर कार्य करते हुये प्रगति करता रहेगा।

सेन्टर की सफलता हेतु मेरी हार्दिक शुभकामनाएं।

(अवनीश कुमार अवस्थी)

"I am delighted to learn about the upward movement of CBMR in top-notch international R&D indices under your able leadership. Your presence and guidance as the Director has brought desired visibility, strengthened research ambience and catalyzed collaborations to the next level of execution. Congratulations to you and to the team CBMR for this marvelous achievement!
We believe that the Center will continue to flourish in emerging and strategic areas of biomedical relevance and align itself well to the national missions of health and well-being. Wishing CBMR the very best."

**Professor Sandeep Verma**
Secretary
Science and Engineering Research Board
Department of Science & Technology,
Government of India, New Delhi

---

**Dr. C.M. Gupta**
Chairman, SAC, CBMR and
Distinguished Professor
Institute of Bioinformatics and
Applied Biotechnology,
Bengaluru

"I am very happy to learn that CBMR performance has been rated as world-class, as per Nature Index 2020-21. It has all been possible due to a highly dedicated and visionary group of brilliant Researchers working at the CBMR and also the high encouragement and freedom given by the present and past directors. I have high appreciation for all the CBMR researchers for putting the Centre on the world map, and congratulate them as well as the Director for this wonderful achievement. My Heartiest Congratulations !!!"

---

"I am happy to know that Centre of Bio-medical Research (CBMR) is listed in the Nature Index 2020-21 global ranking. I heartily congratulate you for the achievement. I am sure, under your dynamic and charismatic leadership CBMR will reach new heights."

**Professor S.K. Barik**
Director
CSIR-National Botanical Research Institute
Lucknow

# Highlighted Articles

Dr. Buddhadeb Chattopadhyay, Assistant Professor

J Am Chem Soc. 2021 Apr 7;143(13):5022-5027. doi: 10.1021/jacs.0c13415. Epub 2021 Mar 30.

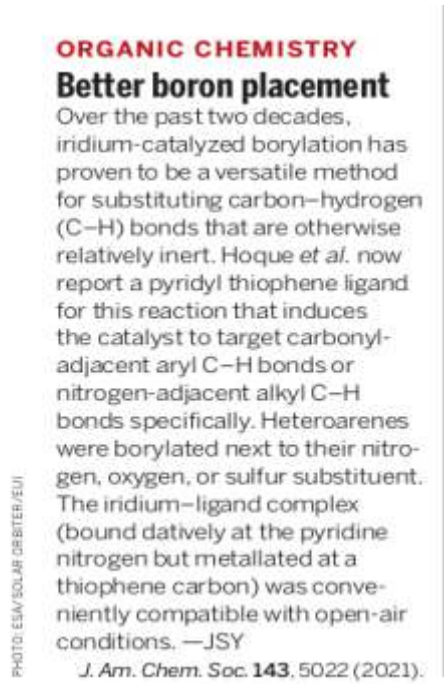
## Remarkably Efficient Iridium Catalysts for Directed C(sp$^2$)-H and C(sp$^3$)-H Borylation of Diverse Classes of Substrates

Md Emdadul Hoque [1], Mirja Md Mahamudul Hassan [1], Buddhadeb Chattopadhyay [1]

Affiliations
PMID: 33783186 DOI: 10.1021/jacs.0c13415

### Abstract

Here we describe the discovery of a new class of C-H borylation catalysts and their use for regioselective C-H borylation of aromatic, heteroaromatic, and aliphatic systems. The new catalysts have Ir-C(thienyl) or Ir-C(furyl) anionic ligands instead of the diamine-type neutral chelating ligands used in the standard C-H borylation conditions. It is reported that the employment of these newly discovered catalysts show excellent reactivity and ortho-selectivity for diverse classes of aromatic substrates with high isolated yields. Moreover, the catalysts proved to be efficient for a wide number of aliphatic substrates for selective C(sp$^3$)-H bond borylations. Heterocyclic molecules are selectively borylated using the inherently elevated reactivity of the C-H bonds. A number of late-stage C-H functionalization have been described using the same catalysts. Furthermore, we show that one of the catalysts could be used even in open air for the C(sp$^3$)-H and C(sp$^2$)-H borylations enabling the method more general. Preliminary mechanistic studies suggest that the active catalytic intermediate is the Ir(bis)boryl complex, and the attached ligand acts as bidentate ligand. Collectively, this study underlines the discovery of new class of C-H borylation catalysts that should find wide application in the context of C-H functionalization chemistry.



ORGANIC CHEMISTRY

**Better boron placement**

Over the past two decades, iridium-catalyzed borylation has proven to be a versatile method for substituting carbon–hydrogen (C–H) bonds that are otherwise relatively inert. Hoque *et al.* now report a pyridyl thiophene ligand for this reaction that induces the catalyst to target carbonyl-adjacent aryl C–H bonds or nitrogen-adjacent alkyl C–H bonds specifically. Heteroarenes were borylated next to their nitrogen, oxygen, or sulfur substituent. The iridium–ligand complex (bound datively at the pyridine nitrogen but metallated at a thiophene carbon) was conveniently compatible with open-air conditions. —JSY

*J. Am. Chem. Soc.* **143**, 5022 (2021).

PHOTO: ESA/SOLAR ORBITER/EUI

May 21, 2021

Science

**Better boron placement**

Jake Yeston

*Science* **372** (6544), 804-805.
DOI: 10.1126/science.372.6544.804-d

# Dr. Syed Masood Husain, Associate Professor

ChemComm

ROYAL SOCIETY OF CHEMISTRY

COMMUNICATION

## Chemoenzymatic, biomimetic total synthesis of (−)-rugulosin B, C and rugulin analogues and their biosynthetic implications†

Amit Mondal, Shailesh Kumar Singh, Tanaya Manna and Syed Masood Husain *

Check for updates

Cite this: *Chem. Commun.*, 2020, 56, 3337

Received 16th January 2020,
Accepted 13th February 2020

DOI: 10.1039/d0cc00406e

rsc.li/chemcomm

**Herein, we report the chemoenzymatic synthesis of a heterodimeric (−)-rugulosin B, homodimeric (−)-rugulosin C, and several rugulin analogues in three to four steps starting from anthraquinones. This work supports dimerization between variously substituted putative monomeric intermediates during the biosynthesis of naturally occurring (+)-rugulosin B and C.**

Nature produces a large number of homo- and hetero-dimeric natural products with fascinating structures which display a variety of useful biological activities. Among these, modified bisanthraquinones (**1–5** and **7–9**) having five to eight chiral centres isolated mainly from fungi constitute a class of secondary metabolites consisting of two chiral monomeric units bonded together with two to four bonds (Fig. 1). The most abundant is homodimeric (+)-rugulosin (**1**)[1,2] (Fig. 1A) isolated initially from *Penicillium rugulosum* Thom[3a] and later from a dozen of other fungal strains,[2b,c] and is known to play a role as a bioinsecticide[3] along with many other prominent biological activities.[2a,4] The other related but less abundant homodimeric bisanthraquinones such as (+)-rugulosin C (**2**),[5] (+)-2,2′-*epi*-cytoskyrin A (**3**),[6] (−)-flavoskyrin (**4**)[1,7] and (−)-rugulosin (**5**)[1,8] and an exceptional four bonded cage-like compound, rugulin (**7**),[9] have also been isolated from various fungal and lichen species (Fig. 1A). However, more interesting is the existence of heterodimeric bisanthraquinones such as (+)-rugulosin B (**8**) isolated from *Penicillium radicum* FKI-3765-2 which shows antimicrobial activity against methicillin-resistant *Staphylococcus aureus*[9] and (−)-deoxyluteoskyrin (**9**) isolated from *Penicillium islandicum* (Fig. 1B).[3] All these natural products appear to be biosynthesized by a unifying strategy that involves the dimerization of chiral monomeric anthraquinone units, as proposed by Shibata and others.[10–12] Although the total synthesis of (+)-rugulosin (**1**) and (+)-2,2′-*epi*-cytoskyrin A (**3**) was successfully demonstrated by the group of Nicolaou,[13a] a much simpler chemoenzymatic, biomimetic, and protecting group free synthesis of their enantiomers, (−)-rugulosin (**5**) and (−)-2,2′-*epi*-cytoskyrin A (**6**), has been reported by us (Fig. 1A).[14]

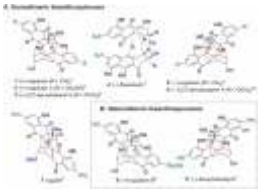


Fig. 1 (A) Homodimeric bisanthraquinones **1–5** and **7** isolated from various fungal species and not yet isolated analogue **6** and (B) heterodimeric bisanthraquinones **8** and **9** isolated from fungi.

In the current work, we envisaged a biomimetic, chemoenzymatic strategy for the preparation of (−)-rugulosin C (*ent*-**2**), (−)-rugulosin B (*ent*-**8**) and rugulin analogues, in just three and four steps, respectively. In order to simplify our strategy, at first, a retro(bio)synthetic route to rugulin type compounds has been proposed (Scheme 1). The rugulin analogue **10** with four C–C bonds might be formed by the oxidative coupling of a dimeric rugulosin type molecule **11**. Based on the earlier proposals by Shibata, **11** can be formed using flavoskyrin type compound **12** following a rearrangement through a number of dimeric intermediates.[10,11] The formation of **12** will require dimerization of monomeric intermediate **13b**, a dienone tautomer of **13a** *via* a hetero-Diels–Alder reaction, whereas **13a**/**13b** appear formed by the enzymatic reduction of anthraquinones (Scl

*Molecular Synthesis and Drug Discovery Unit, Centre for Biomedical Research, Sanjay Gandhi Postgraduate Institute of Medical Sciences Campus, Raebareli Road, Lucknow 226014, India. E-mail: smhusain@cbmr.res.in, smhusain.cbmr@gmail.com*

† Electronic supplementary information (ESI) available: Experimental methods and supplementary figures and tables. See DOI: 10.1039/d0cc00406e





Online Version

ROYAL SOCIETY OF CHEMISTRY

Dear Dr Husain,

I am delighted to inform you that your recent article in *ChemComm* titled "Chemoenzymatic, Biomimetic Total Synthesis of (?)-Rugulosin B, C and Rugulin Analogues and its Biosynthetic Implications" has been chosen by chosen by Antonio Echavarren (ICIQ, Spain) to be included in their specially curated collection on "**Natural Product Synthesis**". by Antonio

**Read all the full the collection at rsc.li/CCNatural_Products**

All articles included are free to access until 31 March 2021.

We will be promoting the collection and articles included via social media and in mailings over the coming weeks and would be delighted if you would share this news with your colleagues as well. You can find us on Twitter @ChemCommun or on WeChat using the QR code below. Please do send us details of your social media handles and we will include them in our promotion.

We would like to thank you for your continued support of the journal and look forward to receiving your next submission soon.

With best wishes,
Harriet

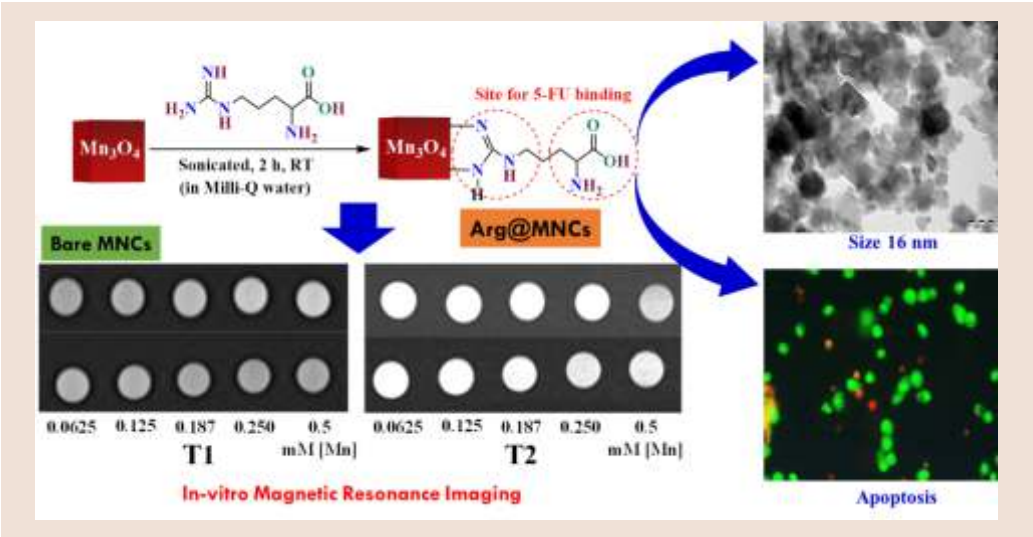
**Dr Harriet Riley**
Deputy Editor, Journals
*ChemComm* | *ChemSocRev*
Royal Society of Chemistry


# Research Highlights

# Modulating the delivery of 5-fluorouracil to human colon cancer cells using multifunctional arginine-coated manganese oxide nanocuboids with MRI properties

5-Fluorouracil (5-FU) is one of the most prescribed drugs and the major component of chemotherapy for the treatment of colorectal cancer. In this study, we have designed arginine-functionalized manganese oxide nanocuboids (Arg@MNCs) for the effective delivery of 5-FU to colon cancer cells. Arginine was used as multifunctional agent to provide stability to MNCs, achieve high drug loading, control the release of loaded drug, and improve delivery to cancer cells. The synthesized Arg@MNCs were characterized by DLS, TEM, XRD, FTIR, XPS, TGA, and VSM analysis. The structural and morphological analysis by TEM showed cuboid-shaped MNCs with average particle size ~15 nm. Biodegradation studies indicated that the Arg@MNCs were degraded at endolyosomal pH in 24 h while remaining stable at physiological pH. Hemolytic toxicity studies revealed the safety and nontoxic nature of the prepared MNCs. 5-FU-loaded Arg@MNCs showed significant control over the release of 5-FU, decrease in the hemolytic toxicity of loaded 5-FU but higher in vitro anticancer activity against HCT 116 and SW480 human colon cancer cells. Importantly, both the bare MNCs and Arg@MNCs showed excellent T1 and T2MR relaxivity under 3.0 T MRI scanner. Thus, the nanostructures developed in this study, i.e., 5-FU-Arg@MNCs could overcome the issues of both MNCs (stability) and 5-FU (low drug loading and nonspecificity) and may be used as a multifunctional theranostic nanocarrier for colon cancer treatment.

Jain P, Patel K, Jangid A K, Guleria A, Patel S, Pooja D and Kulhari H
***ACS Applied Bio Materials*** (2020), 3(10), 6852-6864

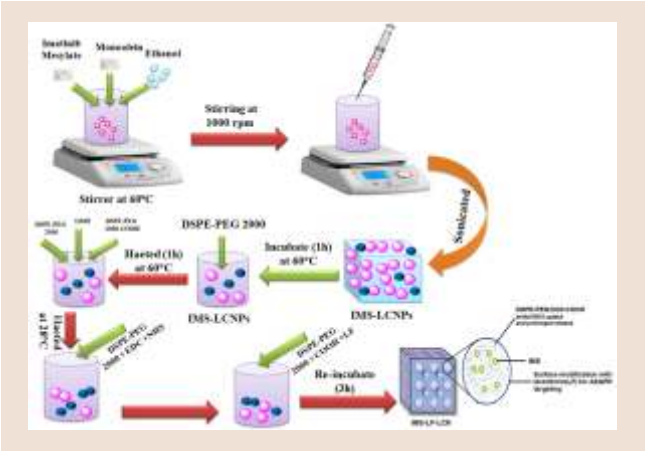



Synthesis of arginine-functionalized manganese oxide nanocuboids (Arg@MNCs) for effective delivery of 5-Fluorouracil

# Fabrication of imatinib mesylate-loaded lactoferrin-modified PEGylated liquid crystalline nanoparticles for mitochondrial-dependent apoptosis in hepatocellular carcinoma

Nisha R, Kumar P, Kumar U, Mishra N, Maurya P, Singh S, Singh P, Guleria A, Saha S and Sara S A
***Molecular Pharmaceutics***
(2020), 18(3), 1102-1120

Hepatocellular carcinoma (HCC) is a major cause of concern as it has substantial morbidity associated with it. Previous reports have ascertained the antiproliferative activity of imatinib mesylate (IMS) against diverse types of carcinomas, but limited bioavailability has also been reported. The present study envisaged optimized IMS-loaded lactoferrin (LF)-modified PEGylated liquid crystalline nanoparticles (IMS-LF-LCNPs) for effective therapy of IMS to HCC via asialoglycoprotein receptor (ASGPR) targeting. Results displayed that IMS-LF-LCNPs presented an optimum particle size of 120.40 ± 2.75 nm, a zeta potential of +12.5 ± 0.23 mV, and 73.94 ± 2.69% release. High-resolution transmission electron microscopy and atomic force microscopy were used to confirm the surface architecture of IMS-LF-LCNPs. The results of cytotoxicity and 4,6-diamidino-2-phenylindole revealed that IMS-LF-LCNPs had the highest growth inhibition and significant apoptotic effects. Pharmacokinetics and biodistribution studies showed that IMS-LF-LCNPs have superior pharmacokinetic performance and targeted delivery compared to IMS-LCNPs and plain IMS, which was attributed to the targeting action of LF that targets the ASGPR in hepatic cells. Next, our in vivo experiment established that the HCC environment existed due to suppression of BAX, Cyt c, BAD, e-NOS, and caspase (3 and 9) genes, which thus owed upstream expression of Bcl-xl, iNOS, and Bcl-2 genes. The excellent therapeutic potential of IMS-LF-LCNPs began the significant stimulation of caspase-mediated apoptotic signals accountable for its anti-HCC prospect. $^{1}$H nuclear magnetic resonance (serum) metabolomics revealed that IMS-LF-LCNPs are capable of regulating the disturbed levels of metabolites linked to HCC triggered through N-nitrosodiethylamine. Therefore, IMS-LF-LCNPs are a potentially effective formulation against HCC.




Synthesis of imatinib mesylate-loaded lactoferrin-modified PEGylated liquid crystalline nanoparticles for treating hepatocellular carcinoma

# An NMR based panorama of the heterogeneous biology of acute respiratory distress syndrome (ARDS) from the standpoint of metabolic biomarkers

Acute respiratory distress syndrome (ARDS), manifested by intricate etiology and pathophysiology, demands careful clinical surveillance due to its high mortality and imminent life support measures. NMR based metabolomics provides an approach for ARDS which culminates from a wide spectrum of illness thereby confounding early manifestation and prognosis predictors. $^{1}$H NMR with its manifold applications in critical disease settings can unravel the biomarker of ARDS thus holding potent implications by providing surrogate endpoints of clinical utility. NMR metabolomics which is the current apogee platform of omics trilogy is contributing towards the possible panacea of ARDS by subsequent validation of biomarker credential on larger datasets. In the present review, the physiological derangements that jeopardize the whole metabolic functioning in ARDS are exploited and the biomarkers involved in progression are addressed and substantiated. The following sections of the review also outline the clinical spectrum of ARDS from the standpoint of NMR based metabolomics which is an emerging element of systems biology. ARDS is the main premise of intensivists textbook, which has been thoroughly reviewed along with its incidence, progressive stages of severity, new proposed diagnostic definition, and the preventive measures and the current pitfalls of clinical management. The advent of new therapies, the need for biomarkers, the methodology and the contemporary promising approaches needed to improve survival and address heterogeneity have also been evaluated. The review has been stepwise illustrated with potent biometrics employed to selectively pool out differential metabolites as diagnostic markers and outcome predictors. The following sections have been drafted with an objective to better understand ARDS mechanisms with predictive and precise biomarkers detected so far on the basis of underlying physiological parameters having close proximity to diseased phenotype. The aim of this review is to stimulate interest in conducting more studies to help resolve the complex heterogeneity of ARDS with biomarkers of clinical utility and relevance.

Viswan A, Singh C, Kayastha A M, Azim A and Sinha N
***NMR in Biomedicine***
(2020), 33(2), e4192

# Serum metabolic profile of septic shock patients based upon co-morbidities and other underlying conditions

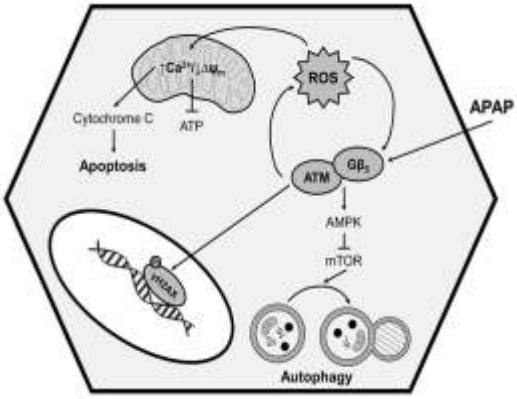
Diagnosis and patient management with septic shock is still a significant challenge for clinicians with its high mortality amongst hospitalized patients. Septic shock is a heterogeneous condition and is usually accompanied by various underlying disease conditions. Dissecting the specific metabolic changes induced by these underlying disease conditions through metabolomics has shown the potential to improve our understanding of the disease's relevant pathophysiological mechanisms, leading to improved treatment. This study has shown the metabolic alterations caused due to co-morbid conditions like diabetes, hypertension, CAD, and CKD in septic shock. It has also shown the distinct metabolic profile of septic shock patients with underlying respiratory illness and encephalopathy. Metabolic profiling of sera obtained from 50 septic shock patients and 20 healthy controls was performed using high-resolution 1D $^{1}$H CPMG and diffusion edited NMR spectra. Univariate and multivariate statistical analysis was performed to identify the potential molecular biomarkers. Noted dysregulations in amino acids, carbohydrate, and lipid metabolism were observed in septic shock patients. Further stratification within the septic shock patients based on co-morbid conditions and primary diagnosis has shown their role in causing metabolic alterations. Evaluation of these compounds during treatment will help design a personalized treatment protocol for the patients improving therapeutics.

Pandey S, Siddiqui MA, Azim A, Trigun SK and Sinha N ***Molecular Omics*** (2020), 17, 260-276

# G protein β5-ATM complexes drive acetaminophen-induced hepatotoxicity

Pramanick A, Chakraborti S, Mahata T, Basak M, Das K, Verma S K, Sengar A S, Singh P K, Kumar P, Bhattacharya B, Biswas S, Pal P B, Sarkar S, Agrawal V, Saha S, Nath D, Chatterjee S, Stewart A and Maity B
***Redox Biology*** (2020), 43, 101965

Excessive ingestion of the common analgesic acetaminophen (APAP) leads to severe hepatotoxicity. Here we identify G protein β5 (Gβ5), elevated in livers from APAP overdose patients, as a critical regulator of cell death pathways and autophagic signaling in APAP-exposed liver. Liver-specific knockdown of Gβ5 in mice protected the liver from APAP-dependent fibrosis, cell loss, oxidative stress, and inflammation following either acute or chronic APAP administration. Conversely, overexpression of Gβ5 in liver was sufficient to drive hepatocyte dysfunction and loss. In hepatocytes, Gβ5 depletion ameliorated mitochondrial dysfunction, allowed for maintenance of ATP generation and mitigated APAP-induced cell death. Further, Gβ5 knockdown also reversed impacts of APAP on kinase cascades (e.g. ATM/AMPK) signaling to mammalian target of rapamycin (mTOR), a master regulator of autophagy and, as a result, interrupted autophagic flux. Though canonically relegated to nuclear DNA repair pathways, ATM also functions in the cytoplasm to control cell death and autophagy. Indeed, we now show that Gβ5 forms a direct, stable complex with the FAT domain of ATM, important for autophosphorylation-dependent kinase activation. These data provide a viable explanation for these novel, G protein-independent actions of Gβ5 in liver. Thus, Gβ5 sits at a critical nexus in multiple pathological sequelae driving APAP-dependent liver damage.

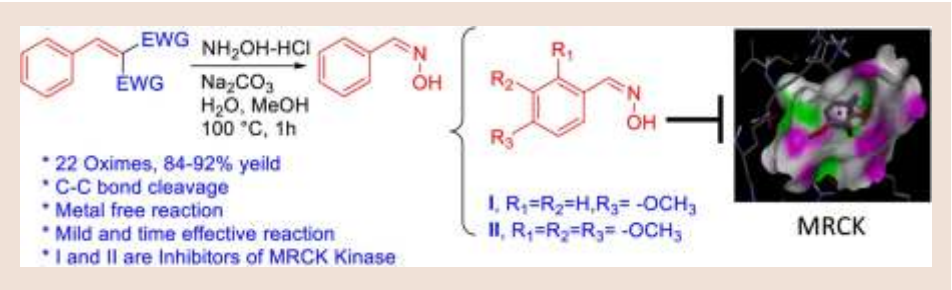



Schematic shows the interaction of G protein β5 and ATM regulates acetaminophen-induced apoptosis and atuophagy

# Water mediated procedure for preparation of stereo Selective oximes as inhibitors of MRCK kinase

Shrivash M K, Singh S, Shukla A K, Luqman S, Pandey J and Misra K
***Journal of Molecular Structure*** (2020), 1220, 128699

Stereoselective aldoximes, preferably Z form have been obtained from α-cyano substituted carbonyl conjugated alkenes. This reaction occurs through Michael addition type reaction followed by retro-Knoevenagel reaction without transition-metal catalysis via C–C bond cleavage. These oximes are evaluated against cancer cell lines employing mechanistic study. Two oximes showed significant cytotoxic activity, which through in silico studies were found to inhibit MRCK Kinase, responsible for metastatic spread of cancer mortality.

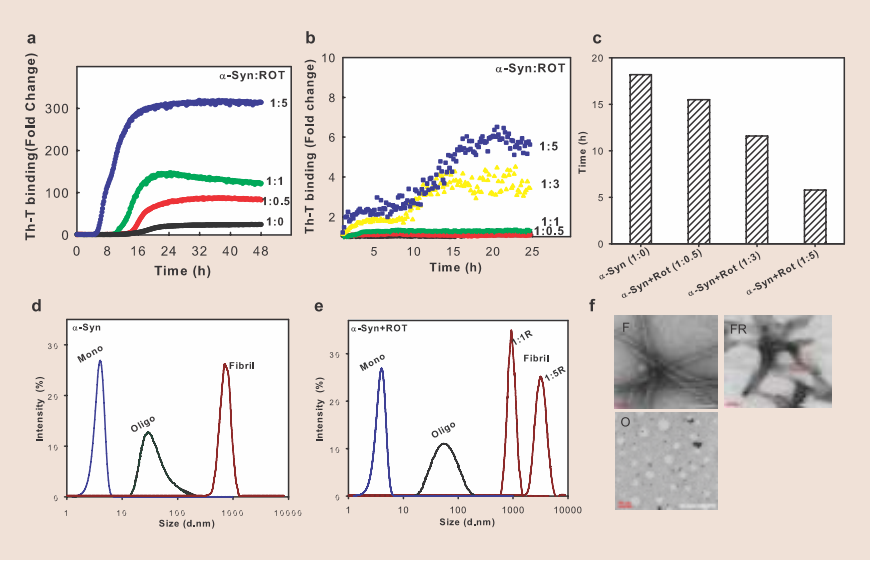



Synthesis of stereo selective oximes as inhibitors of MRCK kinase

# Fast kinetics of environmentally induced α-synuclein aggregation mediated by structural alteration in NAC region and result in structure dependent cytotoxicity

Aggregation of α-synuclein (α-syn) is associated with the manifestation of various pathogenic synucleinopathies, including Parkinson's disease attributed to both genetic and environmental stress factors. The initial events triggering α-syn aggregation and disease initiation due to environmental stress factors are still largely unknown. Here, to understand the mechanism of misfolding and aggregation initiation, we induced α-syn aggregation with rotenone, an established chemical inducer of PD like symptoms. We found that rotenone accelerates the formation of structurally distinct oligomers and fibrils that act as templates and increase the formation of conformers capable of spreading to the neighboring neuronal cells. Molecular dynamics simulations and NMR studies revealed the involvement of NAC region and formation of helical conformations resulting in structural variations in oligomers and fibrils. These structural variations affect the cytotoxic potential of oligomers and fibrils, where, the beta sheet rich oligomers and fibrils alter the membrane potential of neuronal cells and lead to early apoptosis. Our results describe the initial mechanistic events in pathogenic protein aggregation, where initial structural alterations in response to external stress factors dictate the toxicity of resulting conformers. This information will further provide insights in the understanding of protein aggregation, disease progression and pathogenesis.

Shrivastava T, Raj R, Dubey A, Kumar D, Chaturvedi R, Sharma S and Priya S
***Scientific Reports*** (2020), 10, 75361

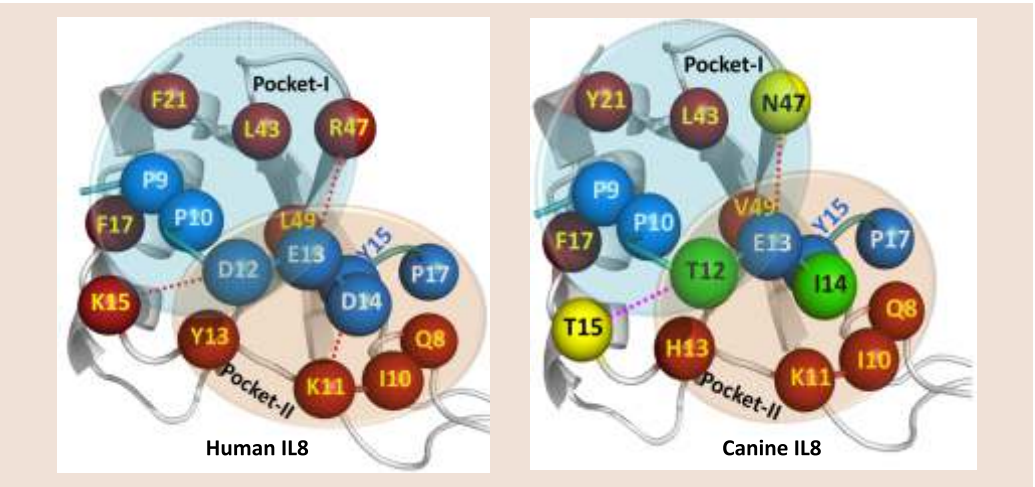



Schematic showing α-synuclein aggregation mediated by structural alteration in NAC region through its binding to rotenone

# Molecular insights into the differential structure-dynamics-stability features of interleukin-8 orthologs: Implications to functional specificity

Gangele K, Gulati K, Joshi N, Kumar D and Poluri KM
***International Journal of Biological Macromolecules***
(2020), 164, 3221-3234

Chemokines are a sub-group of chemotactic cytokines that regulate the leukocyte migration by binding to G-protein coupled receptors (GPCRs) and cell surface glycosaminoglycans (GAGs). Interleukin-8 (CXCL8/IL8) is one of the most essential CXC chemokine that has been reported to be involved in various pathophysiological conditions. Structure-function relationships of human IL8 have been studied extensively. However, no such detailed information is available on IL8 orthologs, although they exhibit significant functional divergence. In order to unravel the differential structure-dynamics-stability-function relationship of IL8 orthologs, comparative molecular analysis was performed on canine (laurasians) and human (primates) IL8 proteins using in-silico molecular evolutionary analysis and solution NMR spectroscopy methods. The residue level NMR studies suggested that, although the overall structural architecture of canine IL8 is similar to that of human IL8, systematic differences were observed in their backbone dynamics and low-energy excited states due to amino acid substitutions. Further, these substitutions also resulted in attenuation of stability and heparin binding affinity in the canine IL8 as compared to its human counterpart. Indeed, structural and sequence analysis evidenced for specificity of molecular interactions with cognate receptor (CXCR1) and glycosaminoglycan (heparin), thus providing evidence for a noticeable functional specificity and divergence between the two IL8 orthologs.

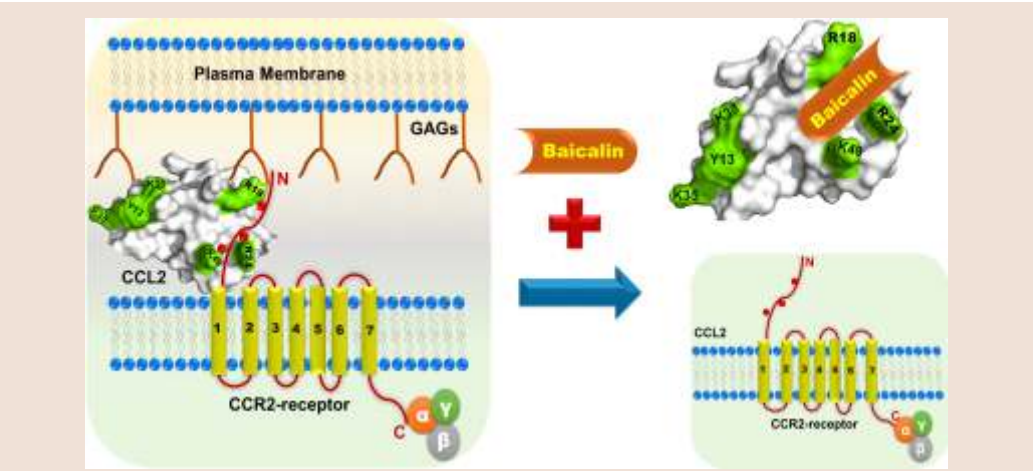



Differential structural regions of human interleukin-8 (IL8) and canine IL8 imparting differential structure dynamic stability to IL8 orthologs

# Elucidating the molecular interactions of chemokine CCL2 orthologs with flavonoid baicalin

An integrated and controlled migration of leukocytes is necessary for the legitimate functioning and maintenance of the immune system. Chemokines and their receptors play a decisive role in regulating the leukocyte migration to the site of inflammation, a phenomena often referred to as chemotaxis. Chemokines and their receptors have become significant targets for therapeutic intervention considering their potential to regulate the immune system. Monocyte chemoattractant protein-1 (MCP-1/CCL2) is a preeminent member of CC chemokine family that facilitates crucial roles by orchestrating the recruitment of monocytes into inflamed tissues. Baicalin (BA), a major bioactive flavonoid, has been reported to attenuate chemokine-regulated leukocyte trafficking. However, no molecular details pertaining to its direct binding to chemokine(s)/receptor(s) are available till date. In the current study, using an array of monomers/dimers of human and murine CCL2 orthologs (hCCL2/mCCL2), we have shown that BA binds to the CCL2 protein specifically with nanomolar affinity (Kd = 270 ± 20 nM). NMR-based studies established that BA binds CCL2 in a specific pocket involving the N-terminal, β1- and β3-sheets. Docking studies suggested that the residues T16, N17, R18, I20, R24, K49, E50, I51, and C52 are majorly involved in complex formation through a combination of H-bonds and hydrophobic interactions. As the residues R18, R24, and K49 of hCCL2 are crucial determinants of monocyte trafficking through receptor/glycosaminoglycans (GAG) binding in CCL2 human/murine orthologs, we propose that baicalin engaging these residues in complex formation will result in attenuation of CCL2 binding to the receptor/GAGs, thus inhibiting the chemokine-regulated leukocyte trafficking.

Joshi N, Kumar D and Poluri KM
***ACS Omega*** (2020), 5, 22637-22651

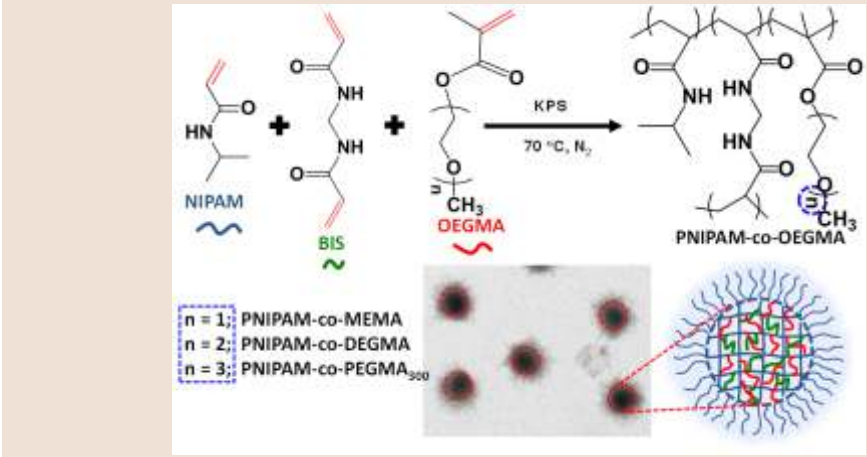



Schematic showing the molecular interactions of chemokine CCL2 orthologs with flavonoid baicalin

# Short oligo(ethylene glycol) chain incorporated thermoresponsive microgels: from structural analysis to modulation of solution properties

Herein, we report synthesis of thermoresponsive poly(N-isopropylaccrylamide) (PNIPAM) microgels with short oligo(ethylene glycol) (OEG) chain comonomers (1 to 4/5 repeating unit) by surfactant-free precipitation copolymerization. The efficient incorporation of the comonomers was confirmed by a complete set of characterization methods viz., FTIR, $^{1}$H NMR, TEM, DLS, and viscometry. The structural heterogeneity and the distribution of the comonomers within the microgels were determined by means of $^{1}$H high-resolution transverse relaxation magnetization measurements. Interestingly, the incorporation of these short OEG chain comonomers led to the formation of a core-corona structure, in which the comonomers were mainly located in the core of the polymeric network with PNIPAM dangling chains at the microgel periphery. The experimental investigations of deswelling behaviours revealed that the OEG chains allowed precise control over the colloidal properties, including phase transition, particles size, swelling degree and polydispersity of the microgels. The tuneability of these properties that was interpreted in terms of polymeric hydrophobic/hydrophilic balance as well as structural diversity, could be achieved by changing the OEG chain length, comonomer feed and crosslinking density. Further, we found that the microgels with more hydrophilic OEG chains were able to show a higher relative swelling, and the same solid content thus led to a higher viscosity at all temperatures. The OEG chains remarkably improved the colloidal stability of the microgels in electrolyte solutions even at higher temperatures, thereby paving the way for the use of these microgels in a range of applications.

Agnihotri P, Raj R, Kumar D and Dan A
***Soft Matter*** (2020), 16, 7845-7859

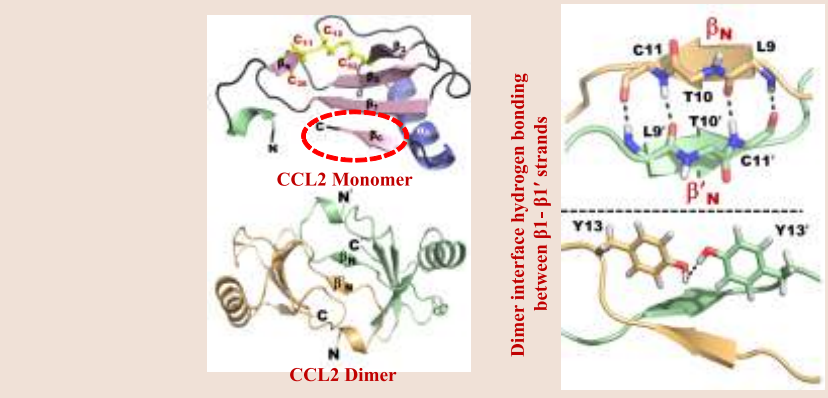



Synthesis of short oligo (ethylene glycol) chain incorporated thermoresponsive microgels for improving its solution properties

# Dissecting the differential structural and dynamics features of CCL2 chemokine orthologs

Chemokines are a sub-group of cytokines that regulate the leukocyte migration. Monocyte chemoattractant protein-1 (MCP/CCL2) is one of the essential CC chemokine that regulates the migration of monocytes into inflamed tissues. It has been observed that the primary sequences of CCL2 orthologs among rodents and primates vary significantly at the C-terminal region. However, no structural details are available for the rodentia family CCL2 proteins. The current study unravelled the structural, dynamics and in-silico functional characteristics of murine CCL2 chemokine using a comprehensive set of NMR spectroscopy techniques and evolutionary approaches. The study unravelled that the N-terminal portion of the murine CCL2 forms a canonical CC chemokine dimer similar to that of human CCL2. However, unlike human CCL2, the murine ortholog exhibits extensive dynamics in the µs-ms timescales. The presence of C-terminal region of the murine CCL2 protein/rodentia family is highly glycosylated, completely disordered, and inhibits the folding of the structured CCL2 regions. Further, it has been observed that the glycosaminoglycan binding surfaces of these orthologs proteins are greatly differed. In a nut shell, this comparative study provided the role of molecular evolution in generating orthologous proteins with differential structural and dynamics characteristics to engage them in specific molecular interactions.

Joshi N, Nagar N, Gulati K, Gangele K, Mishra A, Kumar D and Poluri KM
***International Journal of Biological Macromolecules*** (2020), 156, 239-251




Structural regions of monomeric and dimeric CCL2 unraveled the differential structural and dynamics features of CCL2 chemokine orthologs

# Characterization of $Cu^{2+}$ and $Zn^{2+}$ binding sites in SUMO1 and its impact on protein stability

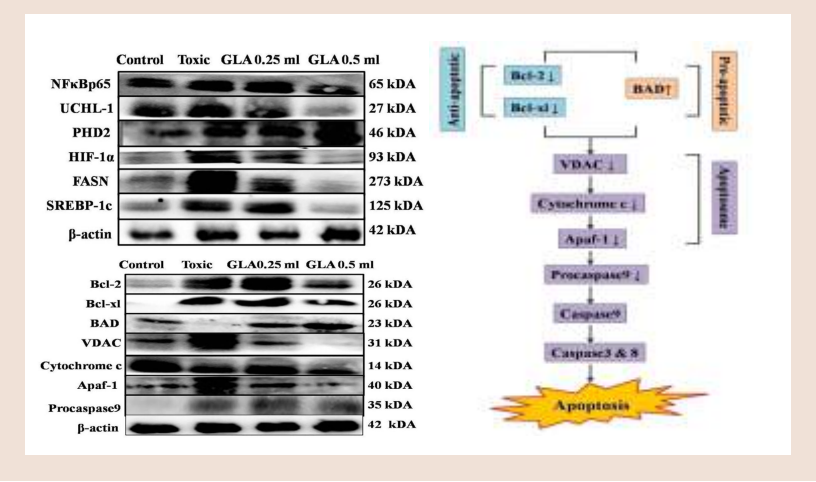
Kaur A, Jaiswal N, Raj R, Kumar B, Kapur S, Kumar D, Gahlay GK and Mithu VS
***International Journal of Biological Macromolecules***
(2020), 151, 204-211

Metal ions like $Cu^{2+}$ and $Zn^{2+}$ have been shown to impact protein misfolding pathways in neurodegenerative proteinopathies like Alzheimer's and Parkinson's. Also, due to their strong interaction with Ubiquitin, they interfere in degradation of misfolded proteins by impairing the ubiquitin-proteasome system (UPS). In this work, we have studied the interaction of these metal ions with a small Ubiquitin like post-translation modifier SUMO1, which is known to work co-operatively with Ubiquitin to regulate UPS system. Between $Cu^{2+}$ and $Zn^{2+}$, the former binds more strongly with SUMO1 as determined using fluorescence spectroscopy. SUMO1 aggregates, forming trimer and higher oligomers in presence of $Cu^{2+}$ ions which were characterized using gel electrophoresis, Bradford assay, and transmission electron microscopy. Chemical shift analysis using $^{15}N/^{1}H$ based NMR spectroscopy revealed that SUMO1 retains its structural fold in its trimeric state. $Cu^{2+}$ induced paramagnetic quenching and $Zn^{2+}$ induced chemical shift perturbation of $^{15}N$-$^{1}H$ cross-peaks were used to identify their respective binding sites in SUMO1. Binding sites so obtained were further validated with molecular dynamics studies. Our findings provide structural insights into the SUMO1-$Cu^{2+}$/$Zn^{2+}$ interaction, and its impact on aggregation of SUMO1 which might affect its ability to modify functions of target proteins.

# Mitochondrial apoptosis and curtailment of hypoxia inducible factor-1α/fatty acid synthase: a dual edge sword perspective of gamma linolenic acid in ER+ mammary gland cancer

Gamma linolenic acid (GLA) is a polyunsaturated fatty acid having selective anti-tumour properties with negligible systemic toxicity. In the present study, the anti-cancer potential of gamma linolenic acid and its effects on mitochondrial as well as hypoxia-associated marker was evaluated. The effect of gamma linolenic acid was scrutinised against ER+MCF-7 cells by using fluorescence microscopy, JC-1 staining, dot plot assay and cell cycle analysis. The in vitro results were also confirmed using carcinogen (n-methyl-n-nitrosourea) induced *in vivo* model. The early and late apoptotic signals in the conjugation with mitochondrial depolarisation were found once scrutinised through mitochondrial membrane potential and life death staining after gamma linolenic acid treatment. Gamma linolenic acid arrested the cell cycle in G0/G1 phase with the majority of cell populations in the early apoptotic stage. The translocation of phosphatidylserine was studied through annexin-V FITC dot plot assay. The markers of cellular proliferation (decreased alveolar bud count, histopathological architecture restoration and loss of tumour micro-vessels) were diminished after gamma linolenic acid treatment. Gamma linolenic acid ameliorates the biological effects of n-methyl-n-nitrosourea persuading the mitochondrial mediated death pathway and impeding the hypoxic microenvironment to make a halt in palmitic acid synthesis.

Roy S, Singh M, Rawat AK, Kumar D and Kaithwas G
***Cell Biochemistry & Function*** (2020), 38(5), 591-603

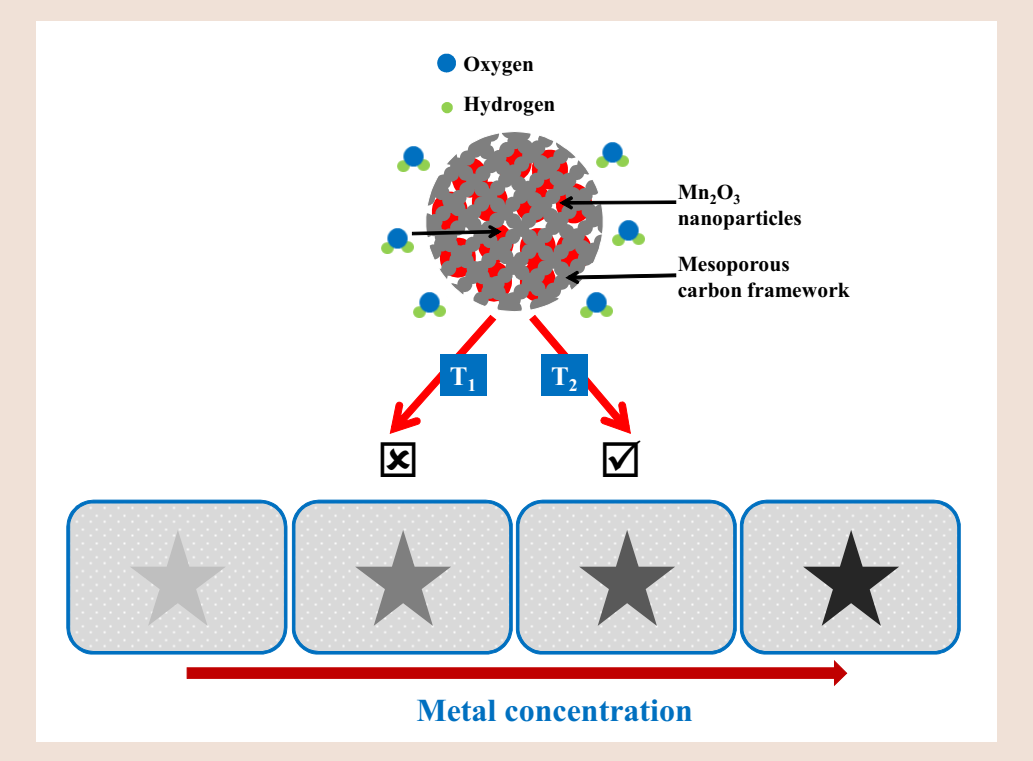



Experimental results showing efficacy of gamma linolenic acid in ER+ mammary gland cancer and its mechanism

# Exclusive T2 MRI contrast enhancement by mesoporous carbon framework encapsulated manganese oxide nanoparticles

Deka K, Guleria A, Kumar D, Biswas J, Lodha S, Kaushik SD, Dasgupta S and Deb P
***Current Applied Physics***
(2020), 20(1), 89-95

Single mode (either T1 or T2) contrast agents employed during magnetic resonance imaging owe their advantage over their dual counterparts to the fact that they do not involve any quenching caused by interference between the two modes. The chemistry involving oxides of manganese is highly significant due to their applicability as MRI contrast agents. Manganese oxides are usually known to display a dominant T1 relaxation enhancement. But, in this work, an engineered structure of manganese oxide ($Mn_2O_3$) nanoparticles encapsulated within mesoporous carbon frameworks was developed which exhibited dominant T2 contrast enhancement, through regulation of contact between the magnetic ion and water. Microstructural characterization revealed that the mesoporous carbon frameworks were spherical in shape and the nanoparticles within them had an average size of 40–50nm. Relaxivity measurement, MRI experiments and cell viability assay convincingly established the system as a new class of biocompatible T2 based magnetic resonance imaging agent.




Schematic showing enhancement of T2 MRI contrast enhancement of mesoporous carbon framework encapsulated manganese oxide nanoparticles

# Mulberries: A promising fruit for phytochemicals, nutraceuticals, and biological activities

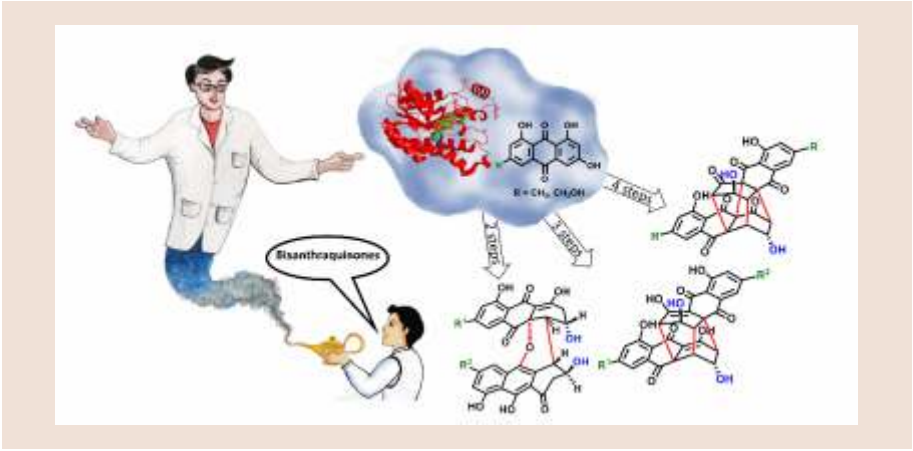
Srivastava D, Singh P, Kumar U, Kumar D, Gosipatalad S B, Saha S, Kumar D and Raj R
***International Journal of Fruit Science*** (2020), 20(3), 1254-1279

The review highlights the significance of mulberry fruits in both chemical and biological sagacity and their role as antioxidant, anticancer, antidiabetic, hepatoprotective, neuroprotective, anti-inflammatory, antiobesity, hypolipidemic, and antibacterial. Besides, having phytochemicals induced biological pathways and nutritional value. Although a number of mulberry fruits species available in nature, the review elucidates the specific role of Morusalba, Morusnigra, Morusrubra, whose functions in living systems are poorly implicit. Many Pharmacological properties of mulberry fruits which are discovered in the recent past for therapeutic purposes also highlighted. Further, ethnopharmacological relevance, medicinal aspects, and bioavailability of mulberry fruits are discussed in detail.

# Chemoenzymatic, biomimetic total synthesis of (-)-rugulosin B, C and rugulin analogues and its biosynthetic implications

Mondal A, Singh SK,
Manna T and Husain SM
***Chemical Communications***
(2020), 56, 3337-3340

A chemoenzymatic method is developed for the synthesis of (−)-rugulosin, (−)-rugulosin C and (−)-rugulosin B and their rugulin analogs. We have shown that by using anthrol reductase from *Talaromyces islandicus* (ARti), we can synthesis (−)-flavoskryins, (−)-rugulosins and (−)-rugulins in just two, three, and four steps, respectively starting from anthraquinones. It further providesthe first evidence in support of the existence homo- as well as heterodimerization between putative biosynthetic intermediates during the biosynthesis of (+)-rugulosin, (+)-rugulosin C and (+)-rugulosin B in *Penicillium radicum* FKI-3765-2. This in contrast to the idea of the modification of (+)-rugulosin (1) to (+)-rugulosin C (2) and (+)-rugulosin B (8) through oxidation. However, an anthrol reductase that can reduce hydroquinones of emodin and citreorosein to the respective, (*S*)-configured dihydroanthracenones and essentially required for the (bio)synthesis of plus enantiomers of the bisanthraquinones is yet to be identified.The procedure developed here will serve as a model for (bio)synthetic studies in the future and may give access to other more complex homo- and heterodimeric bisanthraquinones in a biomimetic fashion.




(−)-Rugulosin B, C and rugulin analogues are synthesized using a chemoenzymatic, biomimetic approach

# New approaches for targeting drug resistance through drug combination

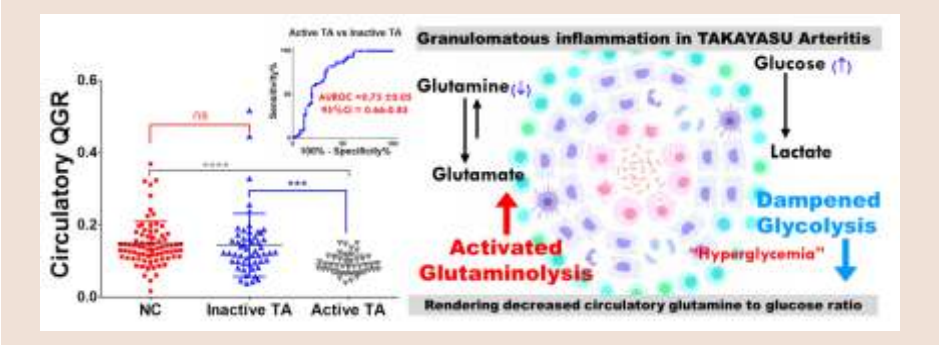
Combination therapy is the tailored use of two or more therapeutic agents and/or methods to counter the rise of multi-drug resistant (MDR) pathogens which is the major health-related issue recognized across the globe. The therapeutic agents such as antibiotics which had been the savior against life-threatening infections, are no longer effective and becoming obsolete. We are left with a limited choice of antibiotics to treat MDR infections instead of their efficacy. While the researchers thrive for the discovery of new antibiotics, combination therapy is also becoming recognized for the management of MDR infections. The application of two or more therapeutic agents with different action mechanisms generates a synergistic effect that is capable of killing MDR pathogens. The pathogen uses its major resources to fight against one agent and simultaneously becomes susceptible to another. Combination therapy provides a broader antimicrobial spectrum, synergistic effects, and minimizes the evolution of drug resistance. However, possible risks of toxicity and super infections are also associated with the excessive use of combination therapy. Scientific advancement in combining the power of drugs with phototherapy and nanotechnology-based treatments are also generating hope for treating MDR infections. The recent development, potential applications, and challenges of combination therapy against multi-drug resistance.

Singh SK, Mohammad A, Alghamdi OA and Husain SM (Book Chapter) ***Combination Therapy Against Multidrug Resistance*** (2020), pp. 221-246; ISBN 9780128205761

# Circulatory glutamine/glucose ratio for evaluating disease activity in Takayasu arteritis: A NMR based serum metabolomics study

The Quantitative assessment of disease activity is important for effective care of patients with Takayasu arteritis (TA). Activated glutaminolysis and reduced glycolytic flux is the hallmark of active inflammation. Based on this, we hypothesize that the circulatory glutamine/glucose ratio (QGR) can serve as an indicant of active inflammation in TA. To probe this hypothesis, the serum samples were collected from 45 active and 53 inactive TA patients fulfilling American College of Rheumatology (ACR) criteria and assessed for disease activity according to Indian Takayasu Clinical Activity Score (ITAS) using acute phase reactant–erythrocyte sedimentation rate [ITAS-A (ESR)]. The quantitative profiles of circulatory metabolites implicated in glutaminolysis (Glutamine and Glutamate) and those which estimate glycolytic flux (i.e. glucose and lactate) were measured using high filed (800 MHz) NMR spectroscopy. The recorded spectra were analyzed using CHENOMX NMR Suite and the estimated concentration profiles were compared and evaluated for their diagnostic potential using Metaboanalyst. Compared to inactive-TA patients, the sera of active-TA patients were characterized by significantly decreased serum levels of glutamine and lactate suggesting that these patients exhibit activated glutaminolysis and reduced glycolytic activity. This is further supported by significantly decreased QGR and lactate to glucose ratio (LGR) levels in active compared to inactive TA patients. The receiver operating characteristic (ROC) curve analysis revealed satisfactory accuracy, sensitivity and specificity for QGR [with area under ROC curve (AUROC) = 0.76 and 95% confidence interval (CI) = 0.66-0.84) compared to that for LGR (with AUROC= 0.67 and CI=0.561-0.77). Therefore, we believe that the circulatory QGR has the potential to serve as surrogate marker for the assessment of disease activity in TA patients. However, the use of this ratio in clinical settings will require future studies on large patient cohorts and procedural optimization as well to improve accuracy.

Kumar U, Jain A, Guleria A, Kumar VR, Misra DP, Goel R, Danda D, Misra R and Kumar D
***Journal of Pharmaceutical and Biomedical Analysis***
(2020), 180, 113080

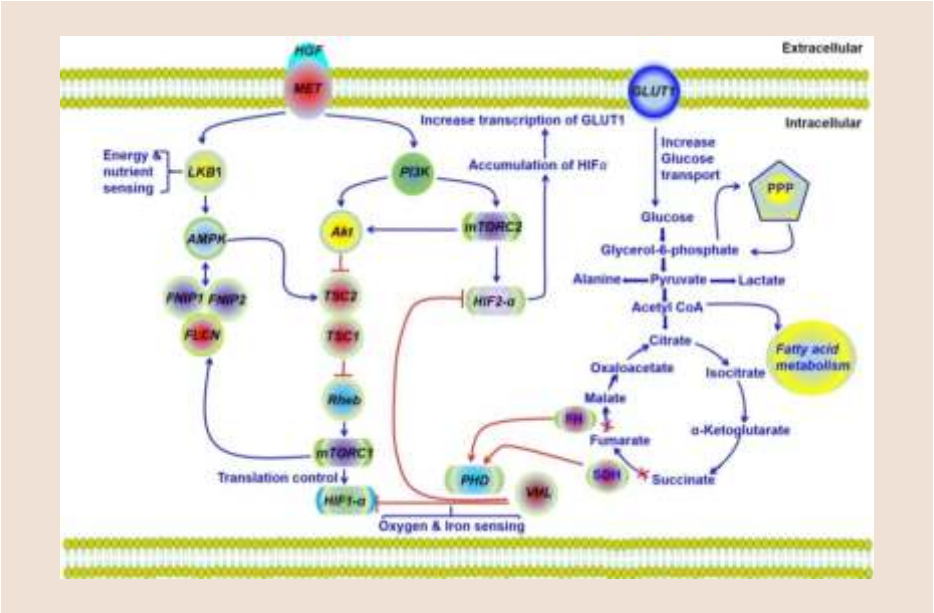



Boxplot comparing the cirulatory levels of glutamine-to-glucose ratio and ROC plot showing its potential in the assessment of disease activity of Takayasu arteritis (TA)

# Role of metabolomics-derived biomarkers to identify renal cell carcinoma: a comprehensive perspective of the past ten years and advancements

Renal cell carcinoma (RCC) is one of the most prevalent metabolic diseases and a leading cause of utmost mortality among men globally. In spite of extensive development in technology for biomarker discovery during the last 10 years, the currently used clinical biomarkers are still unable to detect RCC at early and progression stages. Hence, the development of new and precise biomarkers is most important to improve the clinical management of RCC and reduce the level of mortality. For the detection of RCC at an early stage; a new branch of omics technology - metabolomics - has been introduced. Mainly two techniques (mass spectrometry and nuclear magnetic resonance spectroscopy) have been exploited to execute metabolomics. Precisely, metabolomics showed promising and powerful approach to identify novel RCC biomarker. The review discussed and the literature search to narrate the outcomes of the past 10 years of studies related to RCC pathophysiology, metabolomics, advancements, and shortcomings. Although, compared to mass spectrometric tactic, nuclear magnetic resonance is moving fast to achieve the aim and *in vivo* application for diagnosis and management of RCC, metabolomics-based research in RCC is still in its infancy stage.

Gupta A,Nath K, Bansal N and Kumar K
***Expert Review of Molecular Diagnostics***
(2020), 20(1), 5-18




Schematic showing different pathways associated to RCC and its impact

# White matter alteration in adults with prelingual deafness: A TBSS and SBM analysis of fractional anisotropy data

Kumar, Uttam, Singh A and Mishra M
***Brain and Cognition*** (2021), 148-105676

A loss of this sense in early life leads to diversifications of important white matter networks. Previous studies related to WM alterations in adult deaf individuals mainly involved univariate analysis of fractional anisotropy (FA) data and volumetric analysis, which yielded inconsistent results. To address this issue, we investigated the FA value alterations in 38 prelingual adult deaf individuals and compared the results with those obtained from the same number of adults with normal hearing by using univariate (tract-based spatial statistics) and multivariate (source-based morphometry) methods.The findings from tract-based spatial statistics suggested an increased FA value in regions such as the left cingulate gyrus, left inferior frontal occipital fasciculus, left inferior longitudinal fasciculus and superior corona radiata; however, the results indicated a decreased FA value in the left planum temporale of adult deaf individuals. While source-based morphometry analysis outlined higher FA values in regions such as bilateral lingual gyrus, bilateral cerebellum, bilateral putamen and bilateral caudate, a considerable decrease was observed in the bilateral superior temporal region of the deaf group. These alterations in multiple neural regions might be linked to the compensatory cross-modal reorganizations attributed to early hearing loss.

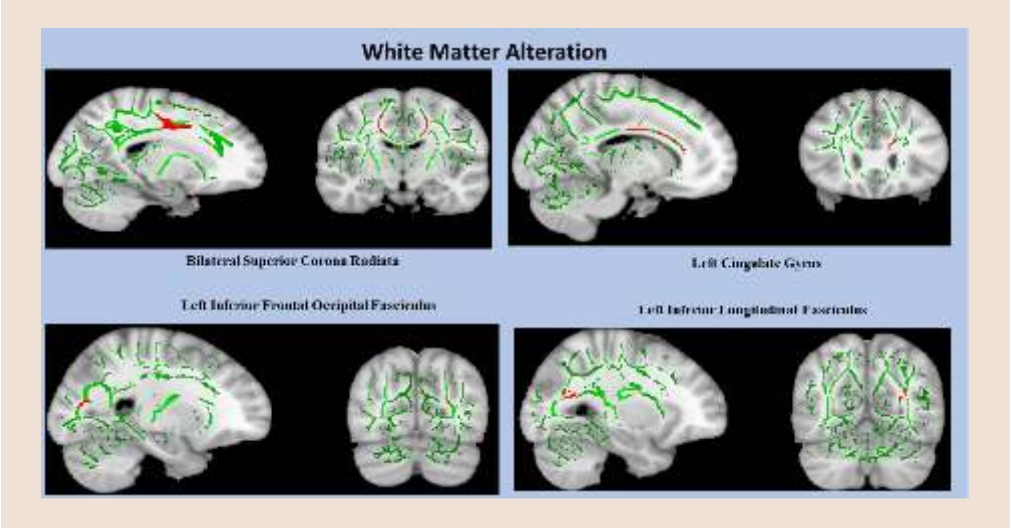



Plate showing alteration in the white matter region in adults with prelingual deafness

# Neural network connectivity in ADHD children: An independent component and functional connectivity analysis of resting state fMRI data

Kumar U, Arya A, and Agarwal V
***Brain Imaging and Behavior*** (2021), 15 (1), 157-165

Resting-state functional magnetic resonance imaging (rsfMRI) is a novel approach that has the potential to examine abnormalities in the default mode network (DMN) component. Two different approaches were used in the present study to characterize the functional connectivities of various DMN components in 16 non-medicated ADHD and a similar number of TD (typically developing) children. rsfMRI data were analysed using independent component analysis (ICA) and region-of-interest (ROI) seed to voxel correlation analysis. ICA results indicated a strong coherence of the left dorsal anterior cingular cortex (dACC) with the DMN components in children with ADHD. In addition, seed-to-voxel functional connectivity analysis using the left dorsal anterior cingulate as a seed region suggested higher temporal coherence with other neural networks upon comparison with TD children. These results imply children with ADHD exhibit a higher dispersed resting state connectivity pattern in DMN and other networks.

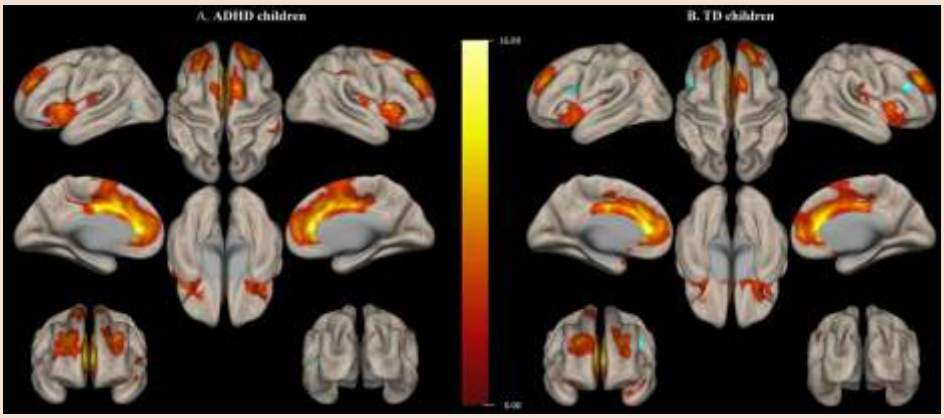
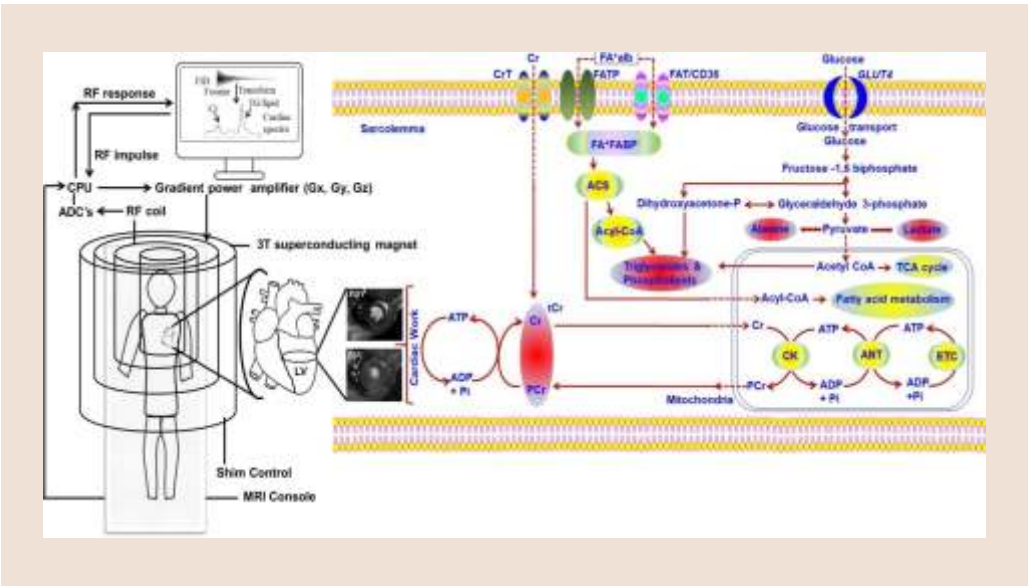



Figure showing the Neural network connectivity in ADHD children evaluated using an independent component and functional connectivity analysis of resting state fMRI data

# Cardiac $^{1}$H MR Spectroscopy: Development of the past five decades and future perspective

Gupta A and Houston B
***Heart Failure Review***
(2021), 26, 839-859

Continued advances in laboratory medicine are required to realize the potential of individualized medicine to impact common cardiovascular diseases. Magnetic resonance imaging (MRI) and spectroscopy (MRS) techniques have advanced over recent years and offer unique, powerful insights into cardiac anatomic and metabolic changes, respectively, occurring in both nascent and advanced heart disease. Although numerous MRI-based in vivo diagnostics are already used in routine clinical practice and more are anticipated, MRS has been less incorporated into routine clinical practice. Given the ability of $^{1}$H MRS to identify and quantify specific molecules with high sensitivity and specificity, its potential utility should be successfully transition from "bench-to-bedside" is tantalizing. The present review will highlight the development of $^{1}$H MRS techniques for cardiac applications, observations in seminal studies with $^{1}$H MRS, and the prospects and challenges for widespread application in patients with cardiovascular disease.

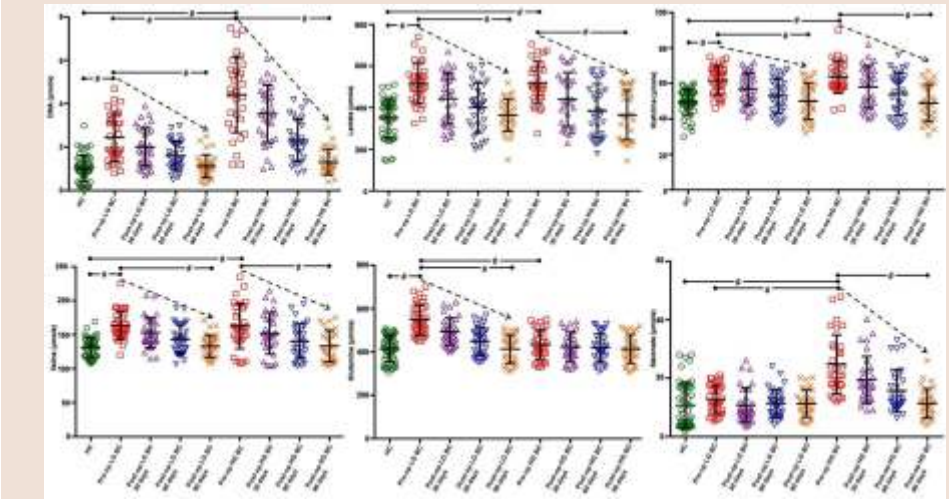



Schematic showing the impact of cardiac $^{1}$H MR spectroscopy in clinical diagnosis

# NMR-derived targeted serum metabolic biomarkers appraisal of bladder cancer: A pre-and post-operative evaluation

Gupta A, Bansal N, Mitash N, Kumar D, Kumar M, Sankhwar SN, Mandhani A and Singh UP
***Journal of Pharmaceutical and Biomedical Analysis***
(2020), 183, 113-134

With high morbidity and mortality, urinary bladder cancer (BC) ranks fifth among common cancers globally. The inherent limitations of urine cytology and cystoscopy, and marginal enhancements in the rate of survival promt us to develop surrogate serum based metabolic biomarkers of screening, identification, and follow-up protocols of management for BC patients. Earlier, we exhibited that abnormal expression levels of dimethylamine (DMA), malonate, lactate, glutamine, histidine, and valine in serum may be used as signature metabolites to differentiate BC from healthy controls (HC). Here we further gauge and validate these observations by comparing pre-operative to post-operative follow-up BC patients. This study was conducted on 160 sera samples involving HC (n = 52), pre-operative (n = 55) and post-operative (n = 53) BC cases. $^{1}$H nuclear magnetic resonance (NMR) spectroscopy was used to generate serum metabolic profiles and to gauge aberrantly expressed metabolites. The targeted metabolomic approach revealed that the expression levels of these signature metabolites were progressively and significantly decreased in post-operative follow-up at the interval of 30, 60, and 90 days compared to pre-operative BC sera samples and were maintained at HC levels. Serum metabolic biomarkers appear to be an inspiring and least-invasive tactic for detection and prognosticating BC patient follow-up.

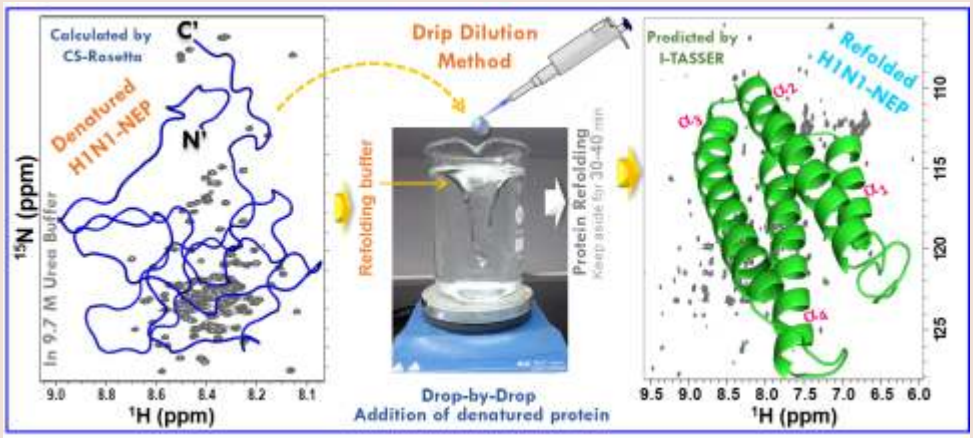


A pre- and post-operative evaluation of NMR-derived targeted serum metabolic biomarkers of bladder cancer

# Instant refolding of nuclear export protein (NEP) from influenza-A virus H1N1 for conducting solution NMR based structural investigations

Jaiswal N, Agarwal N, Poluri KM and Kumar D
***International Journal of Biological Macromolecules*** (2020), 165 (Part B), 2508-2519

Influenza viruses are enveloped viruses of family Orthomyxoviridae and are classified as either type A, B, C, or D. These viruses cause acute respiratory infections and are responsible for seasonal epidemics and occasional pandemics in the human population; thus lending significant morbidity, mortality and economic loss around the world. The primary defense against influenza-A has been vaccination with inactivated or live-attenuated viruses. However, new pandemic strains of influenza can arise either by mutation or re-assortment between human and animal-infecting influenza strains rendering development of new vaccination against newly evolved Influenza-A viral strain. Therefore, at the beginning of a fast-spreading flu pandemic, the antiviral drugs are used to control the flu outcomes as the timely production of sufficient amounts of an effective vaccine always remains a challenge. In the above context, non-structural (NS) proteins have been recognized as potential targets for designing universal anti-influenza drugs.The NS proteins are ubiquitous in all influenza-A virus subtypes and are directly involved in modulating the important aspects of the virus replication cycle, including viral RNA replication, viral protein synthesis, and general host-cell physiology. The genomic segment 8 of influenza A (H1N1) virus encodes two nonstructural proteins: NS1 and NS2 (also known as nuclear export protein, NEP). Of two, the mechanistic structural biology of full length NEP has not been fully characterized so far owing to its tendency to aggregate in solution. As a first step in the direction to study the structural biology of NEP by NMR, we have successful purified the protein NEP using instant-refolding method for the first-time and the underlying mechanism has been rationalized through establishing the complete backbone-resonance-assignments of NEP-N at 9.7M urea-denatured state. The folded NEP protein now will be used for experimental screening of ligands identified as top hits in the virtual screening experiments.




Effect of urea concentration on instant refolding of nuclear export protein (NEP) from influenza-A virus H1N1: A solution NMR based investigation

# Exquisite binding interaction of 18β-glycyrrhetinic acid with histone like DNA binding protein of *helicobacter pylori*: A structure based rational drug discovery approach

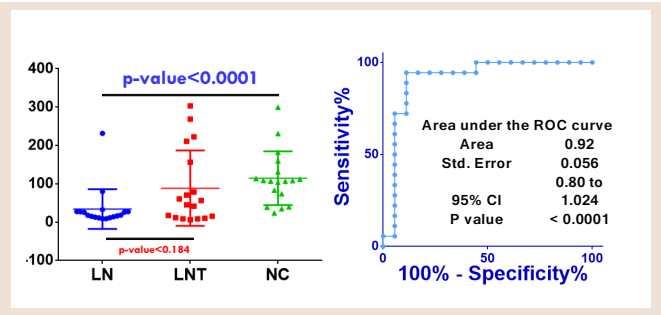
Raj R, Agarwal N, Raghavan S, Chakraborti T, Poluri KM and Kumar D
***International Journal of Biological Macromolecules***
(2020), 161(15), 231-246

*Helicobacter pylori (H. pylori)* is a paradigm for chronic bacterial infections in humans and colonizes the gastrointestinal tract of more than 50% of the world's population. The infection is strongly associated with various gastric diseases including chronic inflammatory gastritis, peptic ulcer, and gastric carcinoma. Due to the emergence of antibiotic resistance, recurrence and increased side effects associated with long-term usage of combination of antibiotics, the efficacy of treatment regimens, used in the treatment of *H. pylori* infections, is seriously challenged in many parts of the world. Therefore, the quest for an alternative treatment strategy free of these inconveniences is currently of utmost clinical interest for eradicating *H. pylori* infections. One of the promising alternatives is to suppress/alter the functioning of Histone-like DNA binding protein of *H. pylori*-referred here as Hup. Hup is a major nucleoid associated protein (NAP) and provides a mechanism for *H. pylori* to survive and colonize persistently under harsh gastric environment because of its remarkable ability to maneuver DNA topology and regulate multiple genes, including those involved in stress response and virulence. Under extreme acidic conditions, it is over expressed by *H. pylori* and protects its genomic DNA through mediating the DNA compaction. However, no attempts have been made, so far, to perturb the functioning of Hup through small molecules. As a first step in this direction, we virtually screened a natural product library containing 56 drug-like bioactive compounds and rationally selected 18β-Glycyrrhetinic acid (GrA) for further computational and experimental testing of its binding interaction with Hup at the molecular level. First, the solution stability of Hup-GrA complex was evaluated using long run molecular dynamics simulations and then fluorescence-quenching and ligand based NMR approaches were used to demonstrate this binding interaction.The various results demonstrate that GrA exhibits an exquisite binding interaction with Hup and would serve as an important molecular scaffold for developing next generation anti-*H. pylori* agents.

# NMR Based targeted urinary profiling of acetate and citrate reveals the effect of cyclophosphamide based induction therapy of lupus nephritis patients

Ganguly S, Kumar U, Gupta N, Guleria A, Majumdar S, Phatak S, Chaurasia S, Kumar S, Aggarwal A, Kumar D and Misra R
***Lupus*** (2020), 29(7), 1-5

The most severe manifestation of Lupus is renal involvement in the form of glomerulonephritis, the condition known as Lupus nephritis (LN). Despite advances in effective immunosuppressive therapies, the treatment of LN remains a challenge with considerably morbidity and progressive end stage renal disease requiring renal replacement therapy. Even major challenge in the management of LN is the assessment of disease activity and monitoring of treatment response. Recently we reported that there is a distinctive reprogramming of the serum metabolomics profile studied by high resolution 800 MHz NMR (nuclear magnetic resonance) spectroscopy following treatment of patients with Lupus Nephritis (LN). As renal functioning directly impacts the urinary profiling, we sought to see if there are urinary parameters as measured by NMR Spectroscopy whose levels parallel with disease activity following 6 months of low dose cyclophosphamide (ELNT) in biopsy proven proliferative lupus nephritis. Urine samples obtained from 18 patients with biopsy proven Lupus Nephritis before and 6 after induction therapy (ELNT) were stored at -80$^{0}$ C and analyzed using high resolution 800 MHz 1D $^{1}$H NMR spectroscopy. Disease activity was measured by SLEDAI. For comparison, the urine samples from 18 normal healthy controls were used (all male and mean age 35). LN patients had a different metabolomic fingerprint as compared with healthy controls with a significantly raised urinary acetate/creatinine levels and a reduced urinary citrate/creatinine levels. The urinary citrate levels (mention the mean levels increased after 6 months of Cylophosphamide treatment whereas urinary acetate showed a trend towards decrease after treatment. The AUC for urinary citrate/creatinine was 0.9136 whereas urinary acetate/creatinine was 0.8086. Correlation analysis between urinary metabolic profiles and clinical parameters (including SLEDAI) was performed further. The urinary acetate levels were significantly correlated with SLEDAI (r=0.337, p=0.048) and urinary citrate levels were significantly correlated with C3(r=0.362,p=0.03) and negatively correlated with uPCR(r=0.346, p=0.039).In conclusion, the decreased urinary citrate level mirrors the finding seen in serum samples of the same patients done earlier which reflects dampened aerobic glycolysis and decreased oxidative phosphorylation. Raised urinary acetate levels are reflective of renal tubular injury and decreased entry into TCA cycle. Thus this approach shows a change in the metabolic profile in response to treatment which can be used as a biomarker for monitoring treatment response.

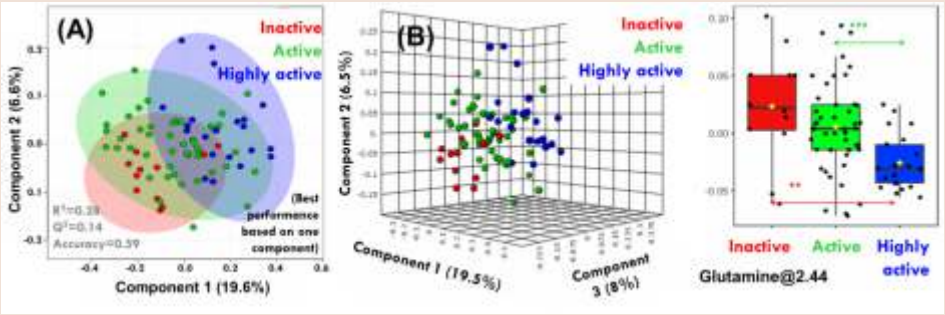



Boxplot comparing the urinary citrate levels before and after the cyclophosphamide therapy in patients with Lupus nephritis

# NMR based clinical metabolomics revealed distinctive serum metabolic profiles in patients with Spondyloarthritis

Spondyloarthritis (SpA) is an umbrella term for autoimmune rheumatic diseases that can affect the back, pelvis, neck and some larger joints, as well as internal organs, like the intestines and eyes. The most common of these diseases is ankylosing spondylitis (ASp) which predominantly affects the spine and sacroiliac joints causing characteristic inflammatory back pain (IBP) and severe spine stiffness. In addition, AsP may involve peripheral joints causing asymmetrical peripheral oligo-arthritis often associated with extra-articular symptoms such as acute anterior uveitis (iritis), psoriasis, enthesitis, dactylitis and chronic inflammatory bowel disease (IBD). These clinical features adversely affect the quality of life in ASp patients owing to restricted spinal/hip mobility, pain, fatigue, disease flares and depression. The clinical management of SpA is marred by delay in diagnosis, and paucity of biomarkers of disease activity. The present study aimed to explore the potential of serum metabolic profiling of patients with SpA to identify biomarker for the diagnosis and assessment of disease activity. The serum metabolic profiles of 81 patients with SpA were compared with that of 86 healthy controls (HC) using nuclear magnetic resonance (NMR) based metabolomics approach. Seventeen patients were followed-up after 3 months of standard treatment and paired sera were analyzed for effects of therapy. Comparisons were done using the multivariate partial least-squares discriminant analysis (PLS-DA) and the discriminatory metabolic entities were identified based on variable importance in projection (VIP) statistics and further evaluated for statistical significance (p-<0.05). We found that the serum metabolic profiles differed significantly in SpA as compared with healthy controls. Compared to HC, the SpA patients were characterized by increased serum levels of amino-acids, acetate, choline, N-acetyl glycoproteins, N-alpha-acetyllysine, creatine/creatinine etc. and decreased levels of low/very-low density lipoproteins, and poly-unsaturated lipids. PLS-DA analysis also revealed metabolic differences between axial and peripheral SpA patients. Further metabolite profiles were found to differ with disease activity and treatment in responding patients. The results presented in this study demonstrate the potential of serum metabolic profiling of SpA as a useful tool for diagnosis, prediction of peripheral disease, assessment of disease activity, and treatment response.

Gupta L, Guleria A, Rawat A, Kumar D and Aggarwal A
***Magnetic Resonance in Chemistry*** (2021), 59 (2), 85-98

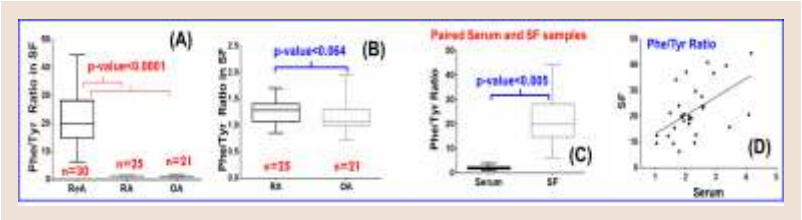



Multivariate (PLS-DA) analysis revealed distinctive serum metabolic profiles in patients with Spondyloarthritis

# Targeted $^{1}$H NMR based metabolomics analysis revealed significantly higher synovial phenylalanine-to-tyrosine ratio in reactive arthritis compared to rheumatoid arthritis and osteoarthritis

Muhammed H, Kumar D, Dubey D, Kumar S, Chaurasia S, Guleria A, Majumdar S, Singh R, Agarwal V and Misra R
***Rheumatology*** (2020), 59(7), 1587-1590

Reactive arthritis (ReA) is an immune mediated inflammatory arthritis condition that develops in response to an extra-articular infection. The development and progression of ReA is closely associated with immune activation and inflammation in the joints (due to SF accumulation) Currently there are no reliable biomarkers in the synovial fluid (SF) available to differentiate reactive arthritis (ReA) from other arthritis conditions. Previous studies have shown the elevated phenylalanine-to-tyrosine ratio (PTR) in infection related clinical conditions which go along with immune activation and inflammation such as sepsis, HIV-1 infection and also in HCV infection under IFN-α therapy.As synovial inflammation in ReA is also an infection mediated immune reaction (cross-reactivity), we hypothesized that the synovial Phe/Tyr ratio in ReA patients will be higher compared to other common arthritis conditions such as Rheumatoid arthritis (RA) and Osteoarthritis (OA). For this, first wemeasured the synovial PTR levels and compared for statistical difference between ReA and non-ReA groups(RA and OA). Evidently, the synovial PTR levelswere significantly higher in ReA patients (mean value = 20.02) compared to both in RA (mean value =1.29) and OA (mean value =1.08) patients suggesting the reduced phenylalanine turnover, possible, due to reduced activity of 5,6,7,8-tetrahydrobiopterin (BH4). BH4 is oxidation-labile cofactor of phenylalanine hydroxylase (PAH); thus PTRlevels not only provide an estimate of enzyme activity of PAH, but, it also serves as surrogate indicator of oxidative stress perpetuating due to immune mediated pro-inflammatory reactions. Compared to ReA patients, the synovial PTR levels were almost comparable in RA and OA patients with p-value <0.064 suggesting low degree of immune mediated oxidative stress in the synovial joints of RA and OA patients. We also compared the PTR values between paired SF and serum samples of ReA patients. Compared to serum, the PTR valueswere significantly higher in the SF suggesting that the immune mediated pro-inflammatory processes are predominantly active in the synovial joints. The PTR valueswere also found to be positively correlated between serum and SF sampleswith regression coefficient ($r^2$) of 0.2873 reflecting the effect of synovial inflammation on the serum metabolic profiles. The present study demonstrates that the synovial PTR profiling might be a useful tool to support the differential diagnosis of ReA from non-ReA conditions.




Metabolomics analysis revealed significantly higher synovial Phe/Tyr ratio in reactive arthritis and undifferentiated spondyloarthropathy and its correlation with serum Phe/Tyr levels

# Investigation of microstructure in poly(methyl methacrylate) prepared via ambient temperature ARGET-ATRP: A combined approach of 1D and 2D NMR spectroscopy

Dhar A, Singh U, Bishnu P Koiry, Baishya B and Haloi DJ ***Journal of Polymer Research*** (2020), 27 (7), 1-8

Poly(methyl methacrylate) (PMMA) has diverse biomaterials applications such as bone cement, bone substitutes, and drug delivery systems. In dental implants, PMMA finds use as missing dental roots.We performed the analysis of different microstructures present in poly(methyl methacrylate) (PMMA) using1D and 2D NMR spectroscopy. The PMMA used in this study was prepared via activators regenerated by electron transfer atom transfer radical polymerization (ARGET-ATRP) in DMF at ambient temperature using methyl 2-chloro propionate (MCP) as initiator, $CuBr_2$ as catalyst in combination with N, N, N′, N′′, N′′-pentamethyldiethylenetriamine (PMDETA) as ligand and ascorbic acid as reducing agent.[13]C NMR, which provides good information about tacticity of a polymer, has been used extensively along with [1]H NMR spectroscopy to extract the information about the different microstructures present in PMMA. Heteronuclear multiple-bond correlation (HMBC), heteronuclear single-quantum coherence (HSQC), and total correlation spectroscopy (TOCSY) were also used to study the position of protons, couplings with carbon etc. in the PMMA.

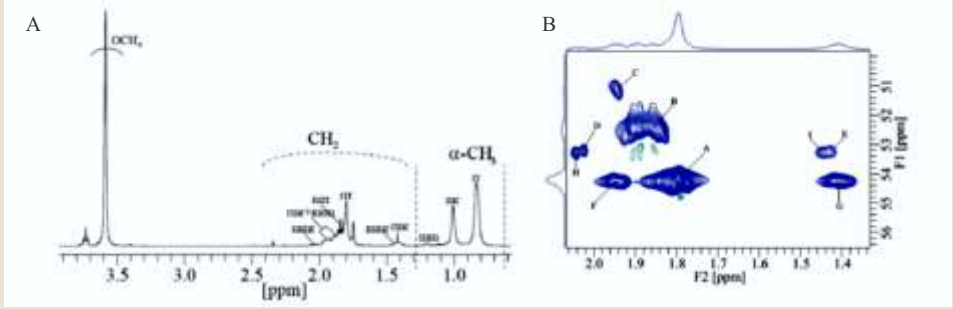
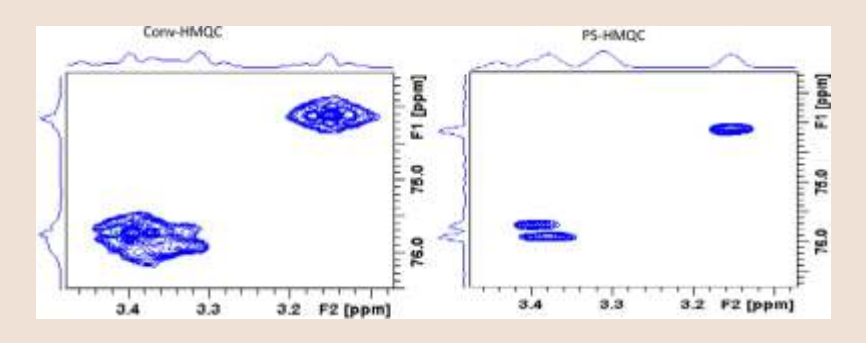



Figure showing (A) [1]H NMR spectrum showing methylene and α-methyl protons of PMMA polymer; (B) The HSQC NMR spectrum of methlene region of poly (methyl methacrylate) (PMMA) polymer

# Pure shift HMQC: Resolution and sensitivity enhancement by bilinear rotation decoupling in the indirect and direct dimensions

Singh U, Bhattacharya S and Baishya B
***Journal of Magnetic Resonance*** (2020), 311, p106684

Spectral overlap often complicates analysis of $^{1}$H NMR spectra of biofluids, complex mixtures, and natural products etc. This hampers identification of biomarker peaks which are related to the pathophysiological sates. Methods for better identification of metabolites are critically important to improve the quality of metabolic profiling and subsequent biological interpretation. There has been significant effort worldwide to improve the resolution of metabolite signals in metabolomics. We developed a technique called pure-shift heteronuclear multiple-quantum correlation (HMQC) NMR for this purpose. The HMQC spectrum displays $^{1}$H-$^{1}$H *J*-multiplets along both dimensions. Thus, multiplets along both dimensions lower the resolution and sensitivity of this technique in detecting small molecules and mixtures. We have implemented a broadband homonuclear decoupling scheme in the HMQC in direct as well as indirect dimension which improves resolution and sensitivity of this technique for detection of small molecules and mixtures.



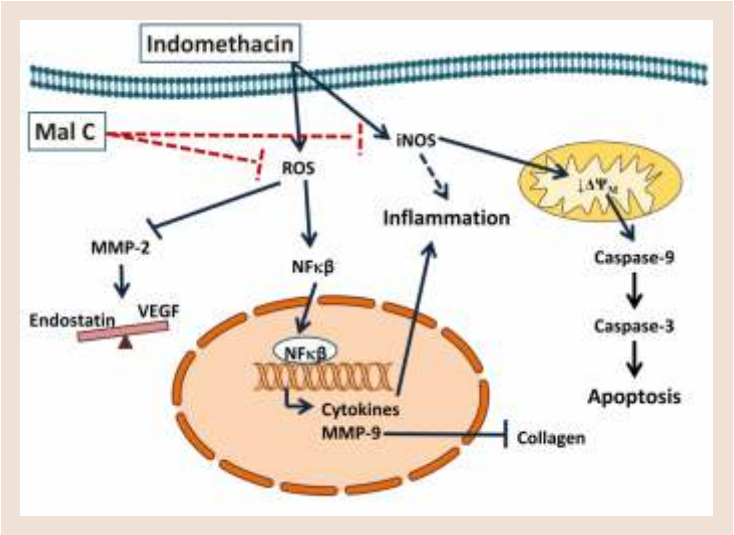

Spectral regions showing improved resolution and sensitivity of pure shift HMQC compared to conventional HMQC

# Malabaricone C attenuates NSAID-induced gastric ulceration by decreasing oxidative/nitrative stress and inflammation and promoting angiogenesis

Non-steroidal anti-inflammatory drugs (NSAIDs), amongst the most commonly used drugs worldwide, are associated with gastrointestinal complications that severely limit the clinical utility of this essential class of pain medications. Here, we mechanistically dissect the protective impact of a natural product, malabaricone C, on NSAID-induced gastropathy. Malabaricone C dose dependently diminished erosion of the stomach lining and inflammation in mice treated with NSAIDs with the protective impact translating to improvement in survival. By decreasing oxidative and nitrative stress, malabaricone C treatment prevented NSAID-induced mitochondrial dysfunction and cell death; NF-κB induction, release of pro-inflammatory cytokines and neutrophil infiltration; and disruptions in the vascular endothelial growth factor/endostatin balance that contributes to mucosal auto-healing. Importantly, malabaricone C failed to impact the therapeutic anti-inflammatory properties of multiple NSAIDs in a model of acute inflammation. In all assays tested, malabaricone C proved as or more efficacious than the current first line therapy for NSAID-dependent GI complications, the proton pump inhibitor omeprazole.

Given that omeprazole-mediated prophylaxis is, itself, associated with a shift in NSAID-driven GI complications from the upper GI to the lower GI system, there is a clear and present need for novel therapeutics aimed at ameliorating NSAID-induced gastropathy. Malabaricone C provided significant protection against NSAID-induced gastric ulcerations impacting multiple critical signaling cascades contributing to inflammation, cell loss, extracellular matrix degradation, and angiogenic auto-healing. Thus, malabaricone C represents a viable lead compound for the development of novel gastroprotective agents.

Basak M, Mahata T, Chakraborti S, Kumar P, Das M, Bandyopdhyay SK, Stewart A, Saha S and Maity B
***Antioxidants & Redox Signaling*** (2020), 32(11), 766-784

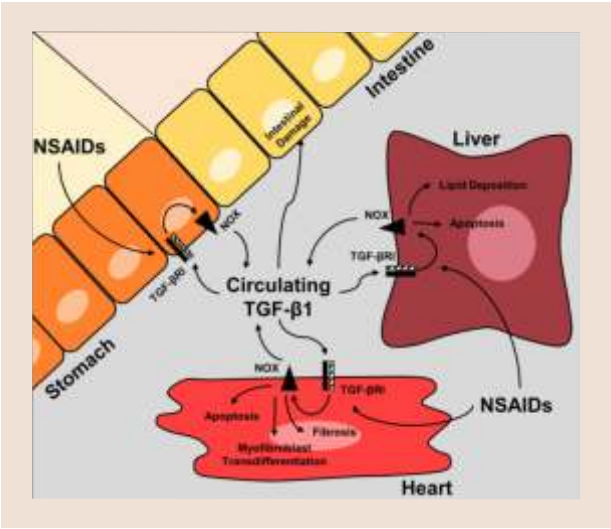



Schematic depicts the mechanism employed by Malabaricone C in reducing oxidative/nitrative stress and inflammation in NSAID-induced gastric ulceration

# Biphasic changes in TGF-β R1 signaling tightly regulates NSAIDs induced multi-organ damage

Chakraborti S, Pramanick A, Saha S, Sarkar S, Stewart A and Maity B
***Free Radical Biology Medicine*** (2020), 160, 125-140

The clinical utility of non-steroidal anti-inflammatory drugs (NSAIDs), used extensively worldwide, is limited by adverse physiological events resulting from chronic drug exposure. Here, we provide evidence identifying transforming growth factor β (TGF-β1), released from multiple tissues, as a critical driver of NSAID-induced multi-organ damage. Biphasic changes in TGF-β1 levels in liver, heart were accompanied by oxidative stress, cell death, fibrotic remodeling, compromised cardiac contractility, and elevated liver enzymes. Pharmacological inhibition of TGF-βRI signaling improved heart, liver function, increased survival of animals exposed to multiple NSAIDs, effects likely mediated by reductions in NOX-ROS generation. Notably, beneficial impact of TGF-βRI blockade was confined to a critical window wherein consecutive, but not concurrent, inhibitor administration improved cardiac, hepatic endpoints. Remarkably, in addition to ameliorating NSAID-mediated myofilament disruptions, cardiac TGF-βRI knockdown lead to lessening in intestinal lesioning underscoring importance of endocrine TGF-β1 signaling in NSAID-tissue injury. Indeed, gastric ulceration was associated with higher incidence of cardiac complications in human cohort underscoring critical importance of circulation-facilitated peripheral organ system interconnectedness in efforts seeking to mitigate toxic side effects of NSAID.

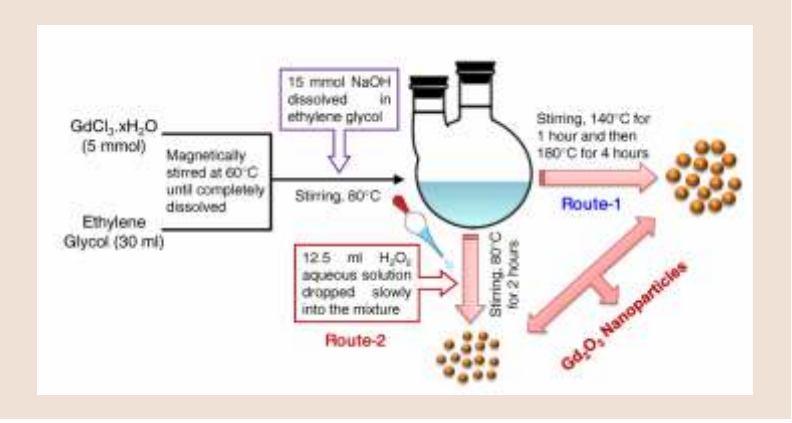



Schematic depicts the intricate mechanism how TGF-beta 1 signaling regulates NSAID-induced multi-organ damage

# *In vitro* and *ex vivo* relaxometric properties of ethylene glycol coated gadolinium oxide nanoparticles for potential use as contrast agents in magnetic resonance imaging

Magnetic nanoparticles (MNPs) have widely demonstrated their applicability in many biomedical applications including magnetic resonance imaging (MRI), hyperthermia, and drug delivery. However, the effectiveness of MNPs can be limited for in vivo applications due to their hydrophobic surfaces leading to nanoparticle agglomeration and thus requires appropriate surface modification to enhance colloidal stability. Glycols are widely used coating material for surface modifications of MNPs to improve their physicochemical properties and biocompatibility. The present work reports the preparation of two different sized ethylene glycol coated gadolinium oxide nanoparticles (EG@Gd2O3 NPs) using two different synthesis approaches and their applicability as contrast agents in MRI. Thermo-gravimetric analysis and Fourier transform infrared spectroscopy confirmed the successful coating of ethylene glycol on the surface of NPs. We found that independent of the size of NPs, the globular shaped EG@Gd2O3 NPs exhibited similar crystal structures, magnetic properties, and cellular cytotoxicity behavior. However, a significant impact of size on MRI contrast enhancement properties was seen. It was revealed that the relaxivity of EG@Gd2O3 NPs increases with a decrease in particle size. Small sized EG@Gd2O3 NPs (~12nm) exhibited a high specific in vitro and ex vivo longitudinal relaxivity of 3.7 and 1.5mM$^{-1}$s$^{-1}$, respectively, thus clearly elucidating the potential of these NPs for use as local contrast enhancement agents. The present study gives insights into the intrinsic dependence of magnetic resonance contrast effects of NPs on particle size and surface coating layer mass ratio and thus demonstrates the development of efficient magnetic nanoparticles based contrast agents by fine tuning of particle size and surface properties.

Chaturvedi A, Pranjali, Kumar M, Meher, Raj R, Basak M, Singh RK, Poluri KM, Kumar D and Guleria A
***Journal of Applied Physics***
(2020), 128, 034903



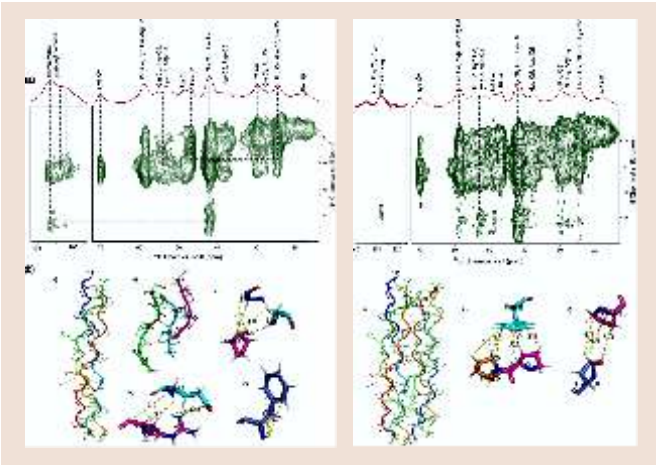

Schematic showing synthetic route of ethylene glycol coated gadolinium oxide nanoparticles and its impact on nanoparticle size

# Water – lipid along with short- and long-range collagen interactions detection in native bone by solid state NMR spectroscopy

The study of structural and dynamical properties of lipid and its associated interaction with different components of bone is essential to understand its role at a different level of bone homeostasis such as bone mineralization andbone metabolism. We have studied the water-dependent dynamical changes observed in lipids (triglycerides)in its absolute native environment inside bone by high-resolution $^{1}H$ solid-state nuclear magnetic resonancespectroscopy (ssNMR). Relaxation measurement ($T_2$ measurement) ssNMR experiments were performed at different levels of water network induced by dehydration and H/D exchange in native bone. Our measurements reflect the changes in the local environment and dynamical properties of triglyceride due to different hydration levels. The present study explains the role of water in stabilizing the structural properties of triglycerides in bone, hence will help understand its pathological role associated with bone physiology and bone disorders. Further, we measured solid-state nuclear magnetic resonance(NMR) experiments using the newly developed BioSolidsCryoProbe™ to access its applicability for elucidating the atomic-level structural details of collagen protein in native state inside the bone. We observed approximately a fourfold sensitivity enhancement in the natural abundance $^{13}C$ spectrum compared with the room temperature conventional solid-state NMR probe. With the advantage of sensitivity enhancement, we have been able to perform natural abundance $^{15}N$ cross-polarization magic angle spinning (CPMAS) and two-dimensional (2D) $^{1}H–^{13}C$ heteronuclear correlation (HETCOR) experiments of native collagen within a reasonable time frame. Due to high sensitivity observed, 2D $^{1}H/^{13}C$ HETCOR experiments have helped in detecting several short and long-range interactions of native collagen assembly, thus significantly expanding the scope of the method to such challenging biomaterials.

Tiwari N,
Rai R and Sinha N
***Solid State Nuclear Magnetic Resonance***
(2020), 107, 10166

Tiwari N, Wegner S
and Hassan A
***Magnetic Resonance in Chemistry*** (2021),
59(2), 99-107

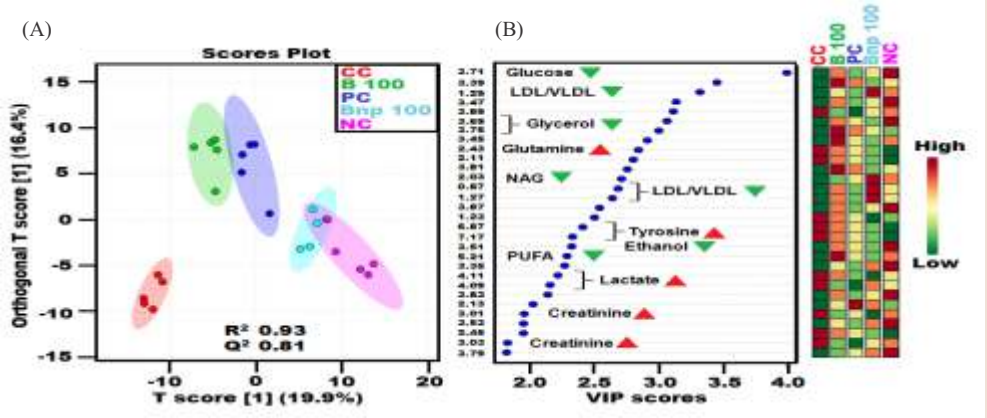


Two-dimensional $^{1}H–^{13}C$ frequency-switched Lee-Goldberg heteronuclear correlation (FSLG-HETCOR) spectrum of native collagen at 500-μs contact time showing various short- and long-range correlation of collagen protein in native bones

# Effect of poly (lactic-co-glycolic acid)-loaded nanoparticles of betulinic acid against hepatocellular carcinoma

Kumar P, Gautam AK, Kumar U, Bhadauria AS, Singh AK, Kumar D, Mahata T, Maity B, Bera H and Saha S
***Archives of Physiology and Biochemistry*** (2020), 6, 1-13

The effectiveness of betulinic acid (B) and PLGA loaded nanoparticles of B (Bnp) against hepatocellular carcinoma (HCC) was established and reported earlier. In continuation of our previous report, the present study described the molecular mechanisms of their antineoplastic responses. In this context, the antineoplastic properties of both B and Bnp were evaluated on DEN-induced HCC rat model. The quantitative real-time polymerase chain reaction and western blot analyses revealed that HCC was developed through lower expressions of e-NOS, BAX, BAD, Cyt C and higher expressions of i-NOS, Bcl-xl, Bcl-2. B and Bnp normalised the expressions of these apoptogenic markers. Particularly, both activated i-NOS and e-NOS mediated Bcl-2 family proteins→ CytC→ Caspase 3 and 9 signalling cascades. The $^{1}$H-NMR-based metabolomics study also demonstrated that the perturbed metabolites in DEN-induced rat serum restored to the normal level following both treatments. Moreover, the antineoplastic potential of Bnp was found to be comparable with the marketed product, 5-flurouracil.

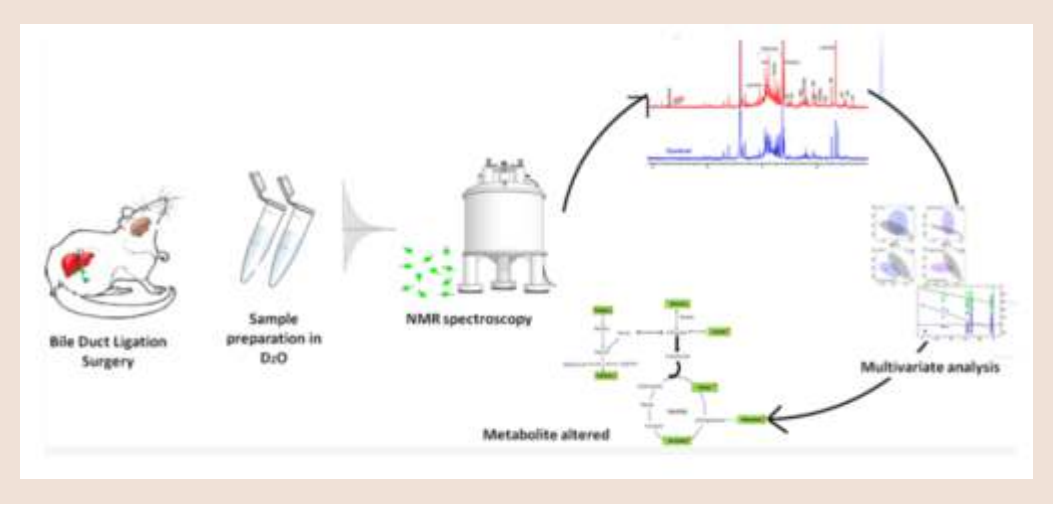



Orthogonal PLS-DA analysis (A) 2D score plot and (B) VIP score plot, showing efficacy of poly (lactic-co-glycolic acid)-loaded nanoparticles of betulinic acid against hepatocellular carcinoma

# $^{1}$H NMR-based metabolic signatures in the liver and brain in a rat model of hepatic encephalopathy

Pathania A, Rawat A, Dahiya SS, Dhanda S, Barnwal RP, Baishya B and Sandhir R
***Journal of Proteome Research*** (2020), 19, 3668-3679

Hepatic encephalopathy (HE) is a debilitating neuropsychiatric complication associated with acute and chronic liver failure. Symptoms includes cognitive and motor deficits. We assessed metabolic alterations in the brain and liver using NMR metabolomics to characterize metabolic signatures associated with HE. The perturbed metabolic profiles in BDL rats relative to control in liver as well as brain were noticed and quantified. Particularly, neurotransmitters such as glutamate and GABA were increased, whereas choline and myo-inositol were decreased. The alterations in neurotransmitter levels resulted in cognitive and motor defects in BDL rats. A significant correlation was found among alterations in NAA/choline, choline/creatine, and NAA/creatine with behavioral deficits. The data suggests impairment in metabolic pathways such as the tricarboxylic acid (TCA) cycle, glycolysis, and ketogenesis in the liver and brain of animals with HE. The study highlights that metabolic signatures could be potential markers to monitor HE progression and to assess therapeutic interventions.




Schematic showing the impact of $^{1}$H NMR based metabolomics in pre-clinical evaluation of hepatic encephalopathy

# Malignancy prediction among tissues from oral SCC patients including neck invasions: a $^{1}$H HRMAS NMR based metabolomic study

Oral cancer is a sixth commonly occurring cancer globally. The use of tobacco and alcohol consumption are being considered as the major risk factors for oral cancer. The metabolic profiling of tissue specimens for developing carcinogenic perturbations will allow better prognosis. To profile and generate precise $^{1}$H HRMAS NMR spectral and quantitative statistical models of oral squamous cell carcinoma (OSCC) in tissue specimens including tumor, bed, margin and facial muscles. To apply the model in blinded prediction of malignancy among oral and neck tissues in an unknown set of patients suffering from OSCC along with neck invasion.

Statistical models of $^{1}$H HRMAS NMR spectral data on 180 tissues comprising tumor, margin and bed from 43 OSCC patients were performed. The combined metabolites, lipids spectral intensity and concentration-based malignancy prediction models were proposed. Further, 64 tissue specimens from twelve patients, including neck invasions, were tested for malignancy in a blinded manner. Forty-eight metabolites including lipids have been quantified in tumor and adjacent tissues. All metabolites other than lipids were found to be upregulated in malignant tissues except for ambiguous glucose. All of three prediction models have successfully identified malignancy status among blinded set of 64 tissues from 12 OSCC patients with an accuracy of above 90%. The efficiency of the models in malignancy prediction based on tumor induced metabolic perturbations supported by histopathological validation may revolutionize the OSCC assessment. Further, the results may enable machine learning to trace tumor induced altered metabolic pathways for better pattern recognition. Thus, it complements the newly developed REIMS-MS iKnife real time precession during surgery.

Paul A, Srivastava S, Roy R, Anand A, Gaurav K, Husain N, Jain S and Sonkar AA
***Metabolomics*** (2020), 16, 38

# $^{1}$H NMR urine metabolomics is an effective prognostic indicator in acute spinal cord injury (ASCI): A prospective case-control study

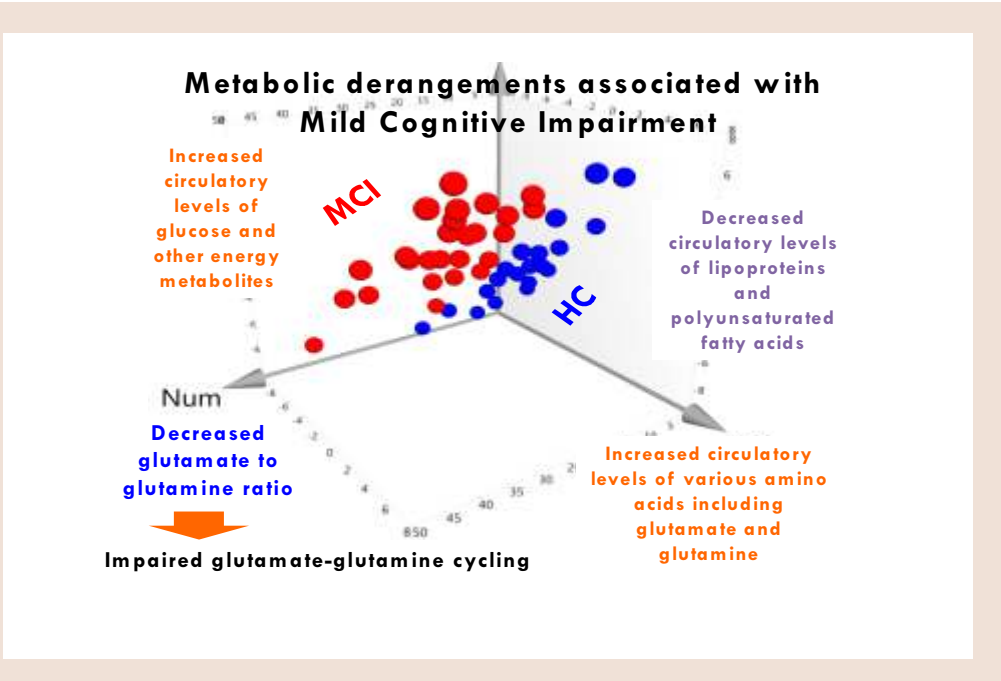
Singh A, Srivastava RN, Chatterji T, Singh S, Raj L, Mahdi A, Garg RK and Roy R
***Journal of Metabolomics and Systems Biology***
(2020), 4(1), 1-21

Acute spinal cord injury (ASCI) is an extremely overwhelming disease with high morbidity and mortality. Despite significant successes in understanding the pathophysiology of ASCI, little is known about limiting neurological damage and predicting recovery. Biofluid metabolomics by $^{1}$H NMR spectroscopy for metabolites quantification specific to nervous tissue injury may determine the injury and progression. This study evaluates the urinary metabolic profile in ASCI cases on two different treatment modalities. One forty participants were enrolled. Group-1, "healthy control, n=70", ASCI cases in Group-2 "fixation with stem cells therapy, n=35" and ASCI cases in Group-3, "fixation alone n=35". Urine samples were collected at baseline and regular follow-ups up to the 6th month for $^{1}$H NMR spectroscopy. The sample spectra were subjected to multivariate Orthogonal Partial Least Square Discriminant Analysis (OPLS-DA) and Variable Importance to the Projection (VIP) analysis. The significant metabolites were correlated with neurological recovery. Acetate, creatinine, creatine, creatine phosphate, urea, and phenylalanine were found to be significant. The 3D scattered score plots in OPLS-DA represented the shifting of cases towards control in the final follow-up. It was further substantiated on VIP score plots. The metabolic aberrations in urine with disease severity in ASCI could be a potential biomarker of neurological recovery.

# An elaborative NMR based plasma metabolomics study revealed metabolic derangements in patients with mild cognitive impairment: A study on north Indian population

Mild cognitive impairment (MCI) is transition phase between cognitive decline and dementia. The current study aims to investigate altered metabolic pattern in plasma of MCI for potential biomarkers. MCI (N =50) and healthy controls (HC, N=50) age group 55–75 years were screened based on Mini Mental State Examination Test (MMSE) and diffusion tensor imaging (DTI imaging). The MMSE score of MCI was significantly lower (25.74±1.83) compared to healthy control subjects (29±1). The MCI patients exhibit significant changes in white matter integrity in the right frontal lobe, right temporal lobe, left frontal lobe, forcep major, fornix, corpus callosum. Further, the plasma samples of twenty seven MCI patients (N =27) and twenty HC subjects (N =20; having no significant differences in any demographics) were analyzed using 1H NMR based metabolomics approach. Consistent with many previous reports, the levels of several plasma metabolites were found to be elevated in MCI patients compared to healthy controls. Further univariate and multivariate ROC curve analyses provided three plasma metabolites as a diagnostic panel of biomarker for MCI; which are lysine, glycine, and glutamine. Overall, the results of this study will help to improve the diagnostic and prognostic strategies of MCI in addition to improving our understanding about disease pathogenesis. We believe that the over-nutritional metabolic phenotype of MCI needs to be targeted for developing future dietary interventions so that the progression of MCI can be limited.

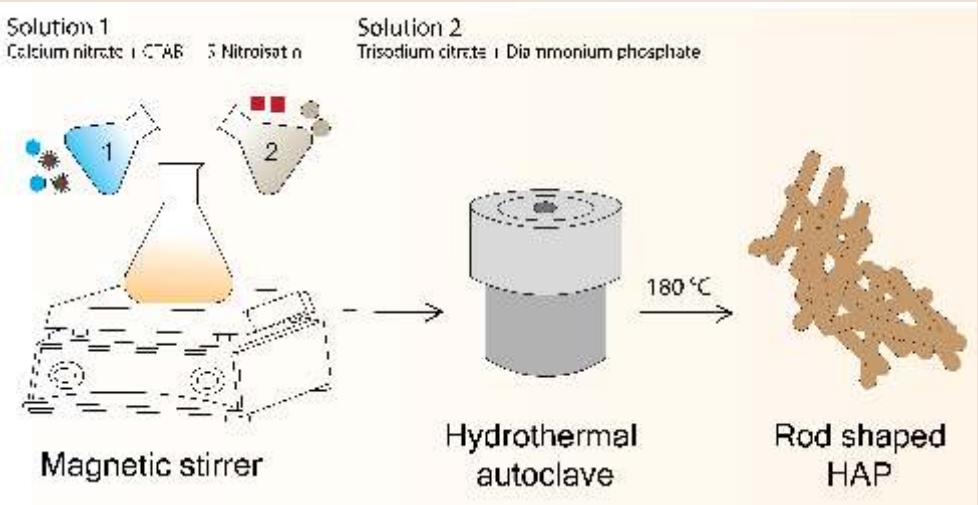
Kumar U, Kumar A, Singh A, Arya P, Singh SK, Chaurasia RN, Singh S, and Kumar D
***Metabolic Brain Disease***
(2021), 36, 957–968



# Incorporation of 5-nitroisatin for tailored hydroxyapatite nanorods and its effect on cervical cancer cells: A nanoarchitectonics approach

Karthick V, Kumar D, Ariga K, Kumar VCM, Kumar VG, Vasanth K, Dhas TS and Ravia M
***Journal of Inorganic and Organometallic Polymers and Materials*** (2021), 31, 1946–1953

Hydroxyapatite (HAP) has been widely used as bone implant for its biocompatibility, and bioactivity. Other approaches like scaffold development, drug delivery and nanomaterials preparation are explored recently. Herein, hydroxyapatite incorporated with 5-nitroisatin (HAP-5 N) was prepared and tested for its anticancer potential. The prepared HAP-5 N has a rod like structure as seen using scanning electron microscopic analysis. The structural elucidation of 5-nitroisatin was confirmed by performing 2D heteronuclear single quantum correlation experiment. The synthesized HAP-5 N was assessed for its possible role as an anticancer agent against cervical cancer (SiHa) cells. The *in-vitro* results shows that HAP-5 N is efficient in inhibiting the growth of cervical cancer cell lines.

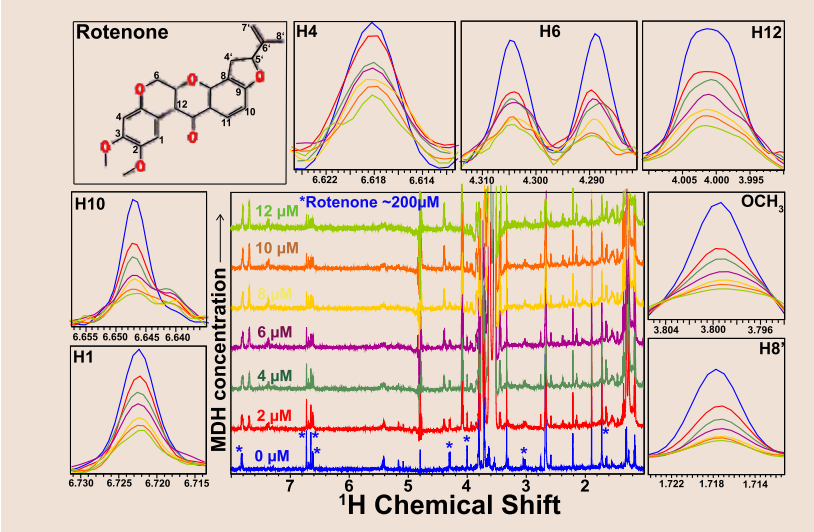



Synthesis of hydroxyapatite nanorods tailored with 5-nitroisatin and its effect on cervical cancer cells

# Pesticide interactions induce alterations in secondary structure of malate dehydrogenase to cause destability and cytotoxicity

Environmental exposure to pesticides increases the risk of neurotoxicity and neurodegenerative diseases. The mechanism of pesticide-induced toxicity is attributed to the increased reactive oxygen species, mitochondrial dysfunction, inhibition of key cellular enzymes and accelerated pathogenic protein aggregation. The structural basis of pesticide-protein interaction is limited to pathogenic proteins such as α-synuclein, Tau and amyloid-beta. However, the effect of pesticides on metabolic proteins is still unexplored. Here, we used rotenone and chlorpyrifos to understand the interaction of these pesticides with a metabolic protein, malate dehydrogenase (MDH) and the consequent pesticide-induced cytotoxicity. We found that rotenone and chlorpyrifos strongly bind to MDH, interferes with protein folding and triggers alteration in its secondary structure. Both pesticides showed high binding affinities for MDH as observed by NMR and LCMS. Rotenone and chlorpyrifos induced structural alterations during MDH refolding resulting in the formation of cytotoxic conformers that generated oxidative stress and reduced cell viability. Our findings suggest that pesticides, in general, interact with proteins resulting in the formation of cytotoxic conformers that may have implications in neurotoxicity and neurodegenerative diseases.

Devi S, Karsauliya K, Srivastava T, Raj R, Kumar D and Priya S
***Chemosphere*** (2021), 263, 128073

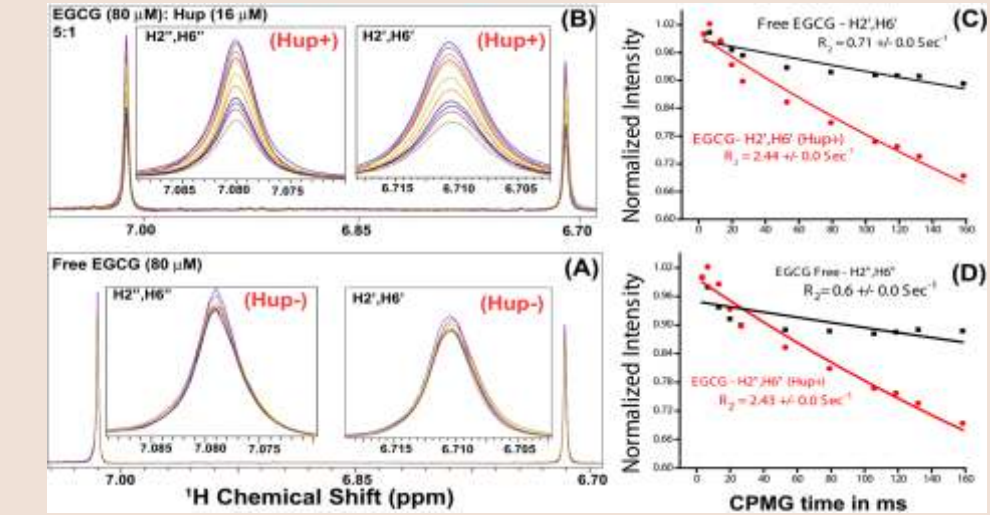



NMR titration experiments showing rotenone interactions with malate dehydrogenase and causing structural changes

# Epigallocatechin gallate with potent anti-*helicobacter pylori* activity binds efficiently to its histone-like DNA binding protein

Raj R, Agarwal N, Raghavan S, Chakraborti T, Poluri K M, Pande G, and Kumar D
***ACS Omega*** (2021), 6 (5), 3548–357

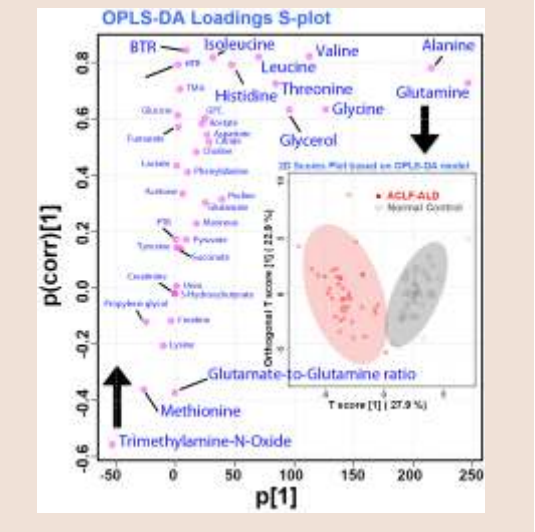
Helicobacter *pylori* (*H. pylori*)—a human gastric pathogen—forms a major risk factor for the development of various gastric pathologies such as chronic inflammatory gastritis, peptic ulcer, lymphomas of mucosa-associated lymphoid tissues, and gastric carcinoma. The complete eradication of infection is the primary objective of treating any *H. pylori*-associated gastric condition. However, declining eradication efficiencies, off-target effects, and patient noncompliance to prolong and broad-spectrum antibiotic treatments has spurred the clinical interest to search for alternative effective and safer therapeutic options. As natural compounds are safe and privileged with high levels of antibacterial-activity, previous studies have tested and reported a plethora of such compounds with potential *in vitro/in vivo* anti-*H. pylori* activity. However, the mode of action of majority of these natural compounds is unclear. The present study has been envisaged to compile the information of various such natural compounds and to evaluate their binding with histone-like DNA-binding proteins of *H. pylori* (referred here as Hup) using in silico molecular docking-based virtual screening experiments. Hup—being a major nucleoid-associated protein expressed by *H. pylori*—plays a strategic role in its survival and persistent colonization under hostile stress conditions. The ligand with highest binding energy with Hup—that is, epigallocatechin-(−)gallate (EGCG)—was rationally selected for further computational and experimental testing. The best docking poses of EGCG with Hup were first evaluated for their solution stability using long run molecular dynamics simulations and then using fluorescence and nuclear magnetic resonance titration experiments which demonstrated that the binding of EGCG with Hup is fairly strong (the resultant apparent dissociation constant (kD) values were equal to 2.61 and 3.29 ± 0.42 μM, respectively).




NMR relaxation experiments showing binding interaction between epigallocatechin gallate with histone-like DNA binding protein (Hup)

# Serum metabolic disturbances associated with acute-on-chronic liver failure in patients with underlying alcoholic liver diseases: An elaborative NMR-based metabolomics study

Acute-on-chronic liver failure (ACLF), which develops in patients with underlying alcoholic liver disease (ALD), is characterized by acute deterioration of liver function and organ failures are secondary to that. The clear understanding of metabolic pathways perturbed in ALD-ACLF patients can greatly decrease the mortality and morbidity of patients through predicting outcome, guiding treatment and monitoring response to treatment.Starting our efforts in this direction, we performed an elaborative NMR-based serum metabolomics analysis and revealed significantly decreased serum levels of various amino acids (except methionine and tyrosine) and those of lipid and membrane metabolites suggested severe nutritional deficiency in ACLF. Serum metabolic features such as branched chain amino acids (BCAAs), BTR (BCAAs to tyrosine ratio), methionine, TMAO, and betaine, were found significantly correlated to severity of hepatic functions as inferred from their statistical correlations with clinical scores such as MELD (Model for End-stage Liver Disease). The ROC curve analysis confirmed the diagnostic potential of these metabolic signatures and their potential utility as biomarker panel for predicting prognosis and monitoring therapeutic response. The various results when compared with previous serum/plasma metabolomics studies involving cirrhotic patients with and without ACLF further confirmed of validity of observed metabolic disturbances. Importantly, the circulatory levels of majority of circulatory amino acids were found to be decreased in the sera of ACLF patients except for methionine which is precursor of S-Adenosylmethionine (SAMe). SAMe serves as the main methylating agent and exerts many key functions in the liver, including serving as a precursor for cysteine, 1 of 3 amino acids of glutathione--the major physiologic defense mechanism against oxidative stress. SAMe is generated by biochemical reaction between methionine and ATP mediated by S-adenosylmethionine synthetase (EC 2.5.1.6; also known as methionine adenosyltransferase (MAT)). The hypermethionemia in ACLF patients might be related to reduced MAT activity and so to progressive liver damage as inferred from its positive correlation with MELD (r=0.21). Therefore, further validation studies on larger prospective cohorts of ACLF patients in a longitudinal manner are crucial to confirm these results and their association with clinical outcomes and severity of hepatic and extra-hepatic impairment.



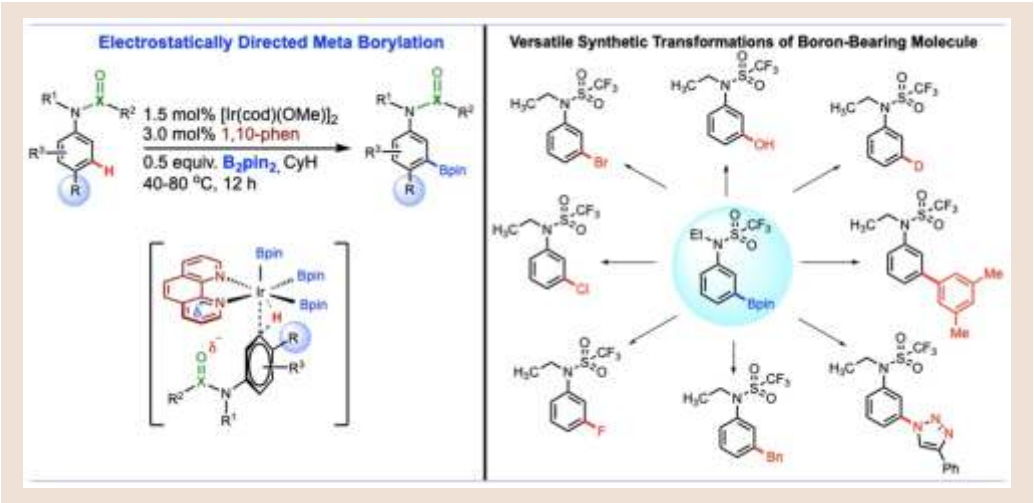

OPLS-DA score plot and loading plots showing metabolic differences in acute-on-chronic liver failure patients compared to normal control subjects

Kumar U, Sharma S, Durgappa M, Gupta N, Raj R, Kumar A, Sharma PN, Krishna VP, Kumar VR, Guleria A, Saraswat VA, Pande G and Kumar D
***Journal of Pharmacy and Bioallied Sciences*** (2021), 13(2), 276-282

# Meta selective C–H borylation of sterically biased and unbiased substrates directed by electrostatic interaction

Chaturvedi J, Haldar C, Bisht R, Pandey G and Chattopadhyay B
***Journal of the American Chemical Society*** (2020), 143, 7604-7611

An electrostatically directed meta borylation of sterically biased and unbiased substrates is described. The borylation follows an electrostatic interaction between the partially positive and negative charges between the ligand and substrate. With this strategy, it has been demonstrated that a wide number of challenging substrates, especially 4-substituted substrates, can selectively be borylated at the meta position. Moreover, unsubstituted substrates also displayed excellent meta selectivity. The reaction employs a bench-stable ligand and proceeds at a milder temperature, precluding the need to synthesize a bulky and sophisticated ligand/template.

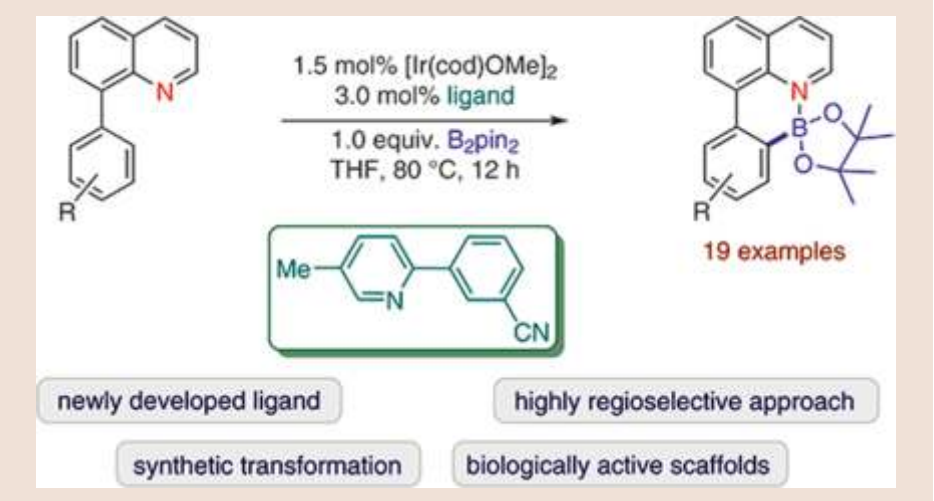



Electrostatic interaction for meta selective C–H borylation

# Iridium-catalyzed site-selective borylation of 8-arylquinolines

Hassan MMM, Hoque M E, Dey S, Guria S, Roy B and Chattopadhyay B
***Synthesis*** (2020), 53(18), 3333-3342

We report a convenient method for the highly site-selective borylation of 8-arylquinoline. The reaction proceeds smoothly in the presence of a catalytic amount of [Ir(OMe)(cod)]2 and 2-phenylpyridine derived ligand using bis (pinacolato) diborane as the borylating agent. The reactions occur with high selectivity with many functional groups, providing a series of borylated 8-aryl quinolines with good to excellent yield and excellent selectivity. The borylated compounds formed in this method can be transformed into various important synthons by using known transformations.




Site-selective borylation of 8-arylquinolines

# Zinc(II)-catalyzed synthesis of secondary amides from ketones via Beckmann rearrangement using hydroxylamine-*O*-sulfonic acid in aqueous media

Verma S, Kumar P, Khatana A K, Chandra D, Yadav A K, Tiwari B and Jat J L
***Synthesis*** (2020), 52(21), 3272-3276

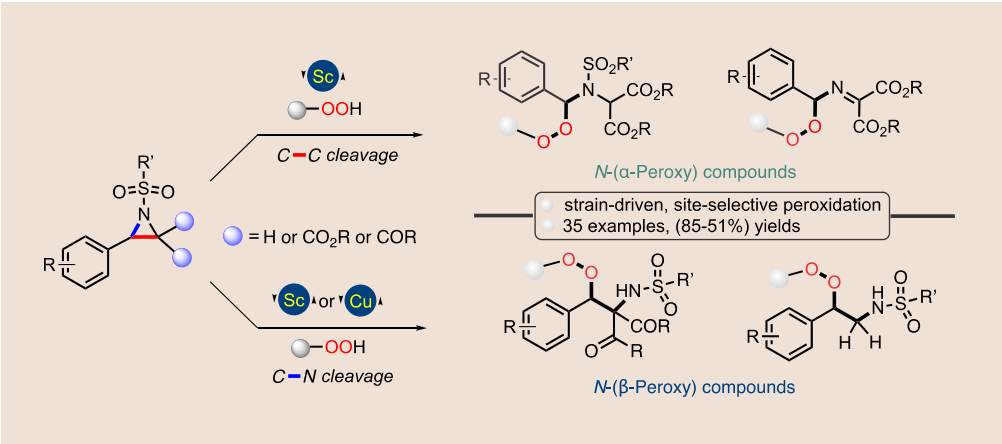
A zinc(II)-catalyzed single-step protocol for the Beckmann rearrangement using hydroxylamine-O-sulfonic acid (HOSA) as the nitrogen source in water was developed. This direct method efficiently produces secondary amides under open atmosphere in a pure form after basic aqueous workup. It is environmentally benign and operationally simple.


Preparation of secondary amides in aqueous media

# An approach to α- and β-amino peroxides via Lewis acid catalyzed ring opening-peroxidation of donor-acceptor aziridines and *N*-activated aziridines

Singh K, Kumar P, Jagadeesh C, Patel M, Das D and Saha J
***Advanced Synthesis and Catalysis*** (2020), 363, 4130-4137

Site selective ring opening process of two different aziridine classes with hydroperoxide is described herein that provides access to various α and β amino and α (imino) peroxy compounds of biological significance. This strain release driven peroxide addition to aziridines represents an alternative approach for entries to biologically significant heteroatom substituted organic peroxides and complements existing methods in the field. The peroxide products obtained by this method displayed a different reactivity during peroxide specific rearrangement processes promoted by either acid or base. Mechanistic studies and useful synthetic elaboration of the products have also been presented.

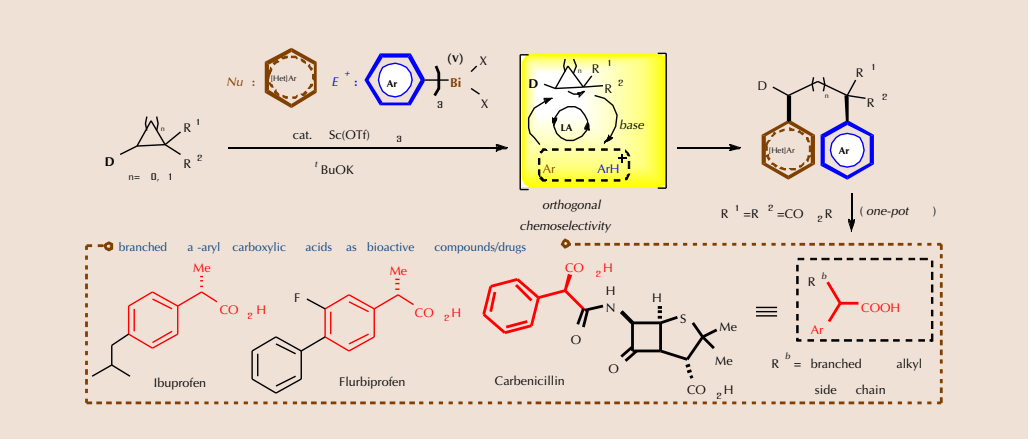



Lewis acid catalyzed ring opening-peroxidation of donor-acceptor aziridines and N-activated aziridines for the synthesis of α- and β-amino peroxides

# Multicomponent, tandem 1,3- and 1,4-bisarylation of donor-acceptor cyclopropanes and cyclobutanes with electron-rich arenes and hypervalent arylbismuth reagents

Mondal B, Das D and Saha J
***Organic Letters*** (2020),
22, 5115-5120

A tandem catalytic process for 1,3- and 1,4-bisarylation of donor−acceptor (D−A) cyclopropanes and cyclobutanes isdisclosed. This strategy capitalizes on the use of two distinct sources of nucleophilic and electrophilic arylating agents, affording theformation of two new C−C bonds in an orchestrated multicomponent fashion with the aid of a catalytic Lewis acid. Mechanisticinvestigations have revealed it to be a stereoselective process, and products could be easily elaborated into other useful compounds. The application of the developed method has been demonstrated with the access of various nonsteroidal anti-inflammatory drugs (NSAID)-analogues.

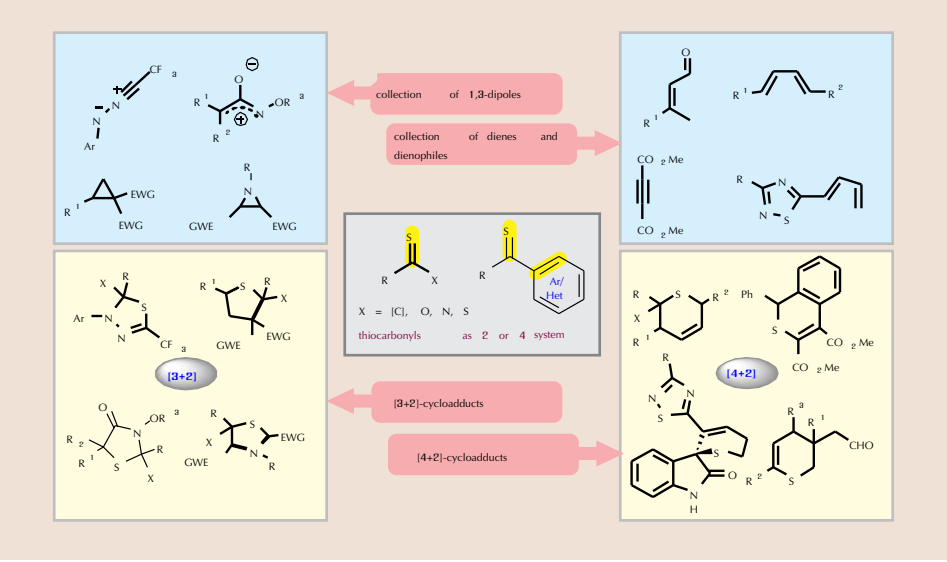



Electron-rich arenes and hypervalent arylbismuth reagets used for multicomponent, tandem 1,3-and 1,4-bisarylation of donor-acceptor cyclopropanes and cyclobutanes

# Recent developments on the synthesis of various sulfur-containing heterocycles via [3+2]- and [4+2]-cycloaddition reactions with thiocarbonyls

Jaiswal V, Mondal B and Saha J.
***Asian Journal of Organic Chemistry*** (2020), 9, 1466-1477

This mini review summarizes important collection of cycloaddition strategies that were used for the synthesis of sulfur containing five and six membered heterocycles from thiocarbonyl based synthons. Among various stepwise or concerted methods available to prepare thioheterocycles, cycloaddition reactions of thiocarbonyls in particular present an important class of reaction owing to their ability to function as super dipolarophiles and/or superdienophiles. Design and development of various reactions in recent years with thiocarbonyls have certainly superseded the general purview on this reactive synthon that it often leads to side reaction and oligomerization. This article, apart from including the advances in the known reaction manifold of thiocarbonyls, also provide updates on new developments of cycloaddition chemistry, which includes donor acceptor (D-A) cyclopropanes and azaoxyallyl cation as 1,3 dipolar reaction partners. This review should serve the purpose of an important guiding tool for organic and medicinal chemist to design and develop new class of cycloaddition or related transformations with thiocarbonyls for the preparation of novel heterocycles.

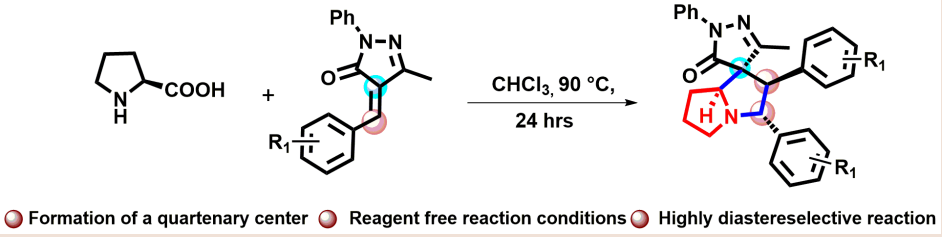



Summary of various sulfur-containing heterocycles via [3+2]- and [4+2]-cycloaddition reactions with thiocarbonyls

# α-Amino acids mediated C–C double bonds cleavage in diastereoselective synthesis of aza-spirocyclic pyrazolones

Awasthi P, Yadav V, Kumar and Tiwari DK
***Advanced Synthesis & Catalysis*** (2020), 362(20), 4378 - 4383

Spiropyrazolones with a spiro-ring fused at 4-position of the pyrazolone core, has received constant attention due to their appearance in a large number of bioactive natural alkaloids and pharmaceuticals that display a wide range of important biological activities such as analgesic, antibacterial, antidiabetic, anti-inflammatory, PPAR α-antagonists, antiviral, anticancer, and type-4-phosphodiesterase inhibitor activities. We developed an efficient and reagent-free method for synthesis of highly functionalized aza-spirocyclicpyrazolones from easily available α-amino acids and alkylidenepyrazolones by means of amination, C-C-double bonds cleavage, and decarboxylative annulation process (Scheme). These highly diastereoselective reactions are promoted simply by α-amino acids and involve in situ generated azomethineylides as reactive intermediates. This newly developed protocol involves the formation of three new bonds (one C-N and two C-C) and four new contiguous stereo-centers including a quaternary carbon center in a single pot cascade process.

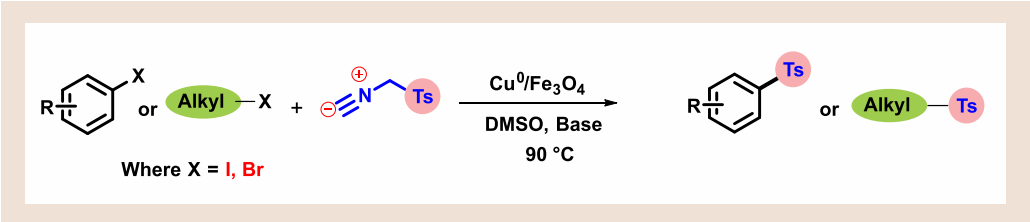



Diastereoselective synthesis of aza-spirocyclic pyrazolones based on α-amino acids mediated C–C double bonds cleavage

# Nano copper-catalyzed synthesis of symmetrical/unsymmetrical sulfones from aryl/alkyl halides and p-toluene sulfonyl-methylisocyanide

Phanindrudu M, Jaya P, Likhar PR and Tiwari DK
***Tetrahedron*** (2020), 76, 131263

TosMIC as a TosylSource: Sulfones containing molecules have medicinal relevance as they are known to possess various activities such as antifungal, anti-HIV, antitumor, and anticancer. We herein, developed a magnetically induced nano copper-catalyzed efficient and mild route for the synthesis of diaryl and alkyl/aryl sulfones from aryl/alkyl halides and tosylmethylisocyanide (TosMIC) (Scheme). A variety of aryl and alkyl sulfones have been obtained in very good to excellent yields. In this newly developed protocol TosMIC acts as sulfonyl source. The catalyst can magnetically be recovered and recycled five times without significant loss in activity.



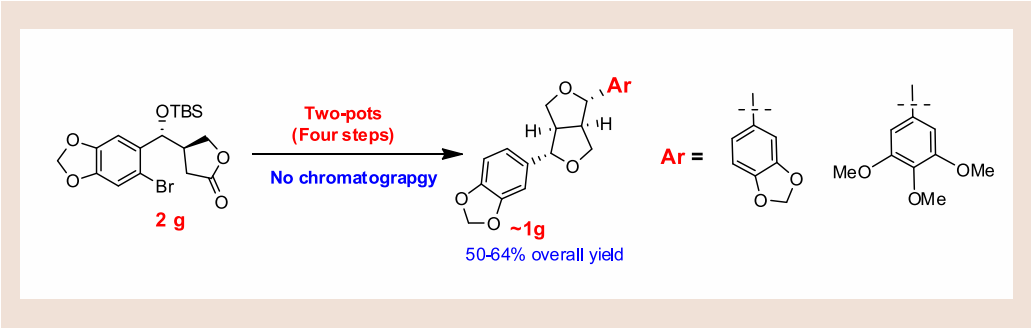

TosMIC as a tosyl source in the synthesis of biaryl and aryl/alkyl sulfones

# Chromatography-free "two-pots" asymmetric total synthesis of (+)-sesamin and (+)-aschantin

Hajra S, Garai S and Sen B
***Tetrahedron*** (2020),
76, 131483

Furofuranlignans are important and the largest subclass of non-butyrolactonelignans isolated from various vascular plants. These lignans are known to exhibit a broad range of biological properties.In 21st century, the modern science and industry are emphasizing on two principal issues “green” and “efficiency” (practicability) for the synthesis of a target compound.

A gram-scale chromatography-free asymmetric total synthesis of both homo- and heterobiarylfurofuranlignans containing at least one methylenedioxy phenyl unit such as (+)-sesamin and (+)-aschantin is accomplished in “two-pots” from easily accessible enantiopure lactone involving four steps in high overall yields. Steps- and pot economy are the key advantages of the protocol. Additionally, the bromo-functionality of the intermediates is useful for late stage functionalization.



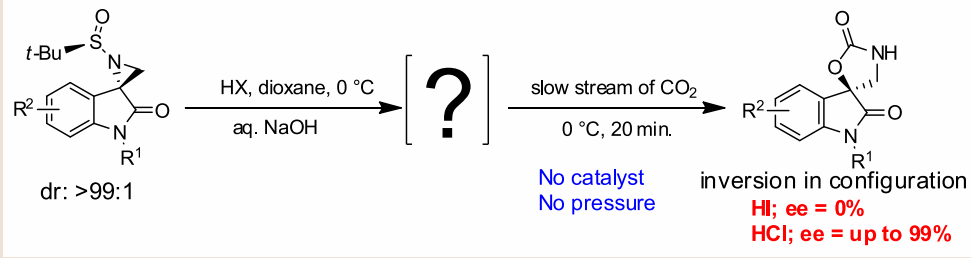

Asymmetric total synthesis of (+)-sesamin and (+)-aschantin based on chromatography-free "two-pots" approach

# Catalyst-free stereocontrolled formal [3+2]-cycloaddition of $CO_2$ for the synthesis of enantiopure spiro [indoline-3, 5'-oxazolidine]-2,2'-diones under aqueous and ambient conditions

Carbon dioxide ($CO_2$) is the most abundant, inexpensive, non-toxic and renewable C1 feedstock. In past decades, chemists and industries have made extensive efforts for the conversion of $CO_2$ into fuels and valuable chemicals. The cycloaddition of $CO_2$ and aziridine for the synthesis of bioactive oxazolidinones is active research area. However, all the chemical fixation of $CO_2$ by aziridine entailed either high pressure, temperature and/or catalyst/additive and mostly under inert conditions. The development of recent and efficient catalyst could improve to the near ambient conditions, but could not avoid the pure $CO_2$ and non-aqueous medium. The catalyst-free cycloaddition of $CO_2$ and aziridine are also reported, but these need either high temperature-pressure or costly dry ice and mechanical energy. The formation of a mixture of regio-isomers of oxazolidinones is another major hitches. Further, the stereoselective chemical fixation of $CO_2$ for the synthesis of enantiopureoxazolidinones is spare in the literature. Spirooxazolidonyloxindoles are found to be important bioactive compounds for example, spirooxazolidione**A** was found to be an indoleamine-2,3-dioxygenase (IDO) inhibitor and **B** could be used as potential nervous system agent

A highly efficient regio- and stereoselective spontaneous formal [3+2]-cycloaddition of $CO_2$ in aqueous medium is developed for the one-pot synthesis of spiro[indoline-3,5'-oxazolidine]-2,2'-diones with excellent enantiopuirity (ee up to 99%) under catalyst-free and ambient conditions. The detailed study reveals NH-spiroaziridine- and 3-(aminomethyl)-3-chloro-oxindoles; two in situ generated reactive intermediate compounds for the spontaneous cycloaddition with $CO_2$ and the latter is responsible for the stereoselectivity. An unprecedented mechanism of desulfinylation is also disclosed herewith.

Hajra S and Biswas A
***Organic Letters*** (2020), 22, 4990-4994

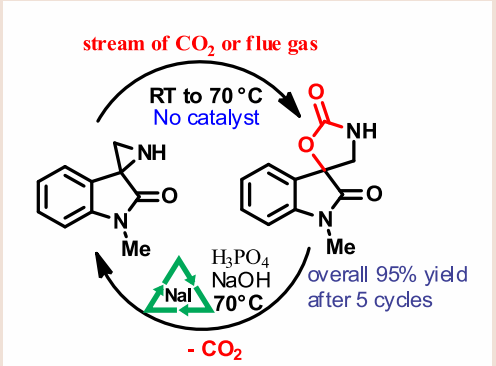


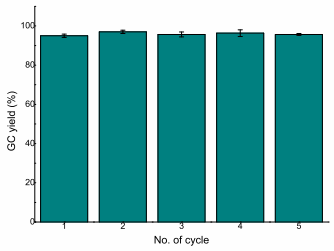

Synthesis of enantiopure spiro [indoline-3, 5'-oxazolidine]-2,2'-diones under aqueous and ambient conditions following catalyst-free stereocontrolled formal [3+2]-cycloaddition of $CO_2$ approach

# Efficient chemical fixation and defixation cycle of carbon dioxide under ambient conditions

Hajra S and Biswas A
***Scientific Reports*** (2020), 10, 15825

Chemical fixation of $CO_2$ as a C1 feedstock for producing value-added products is an important post-combustion technology reducing the $CO_2$ emission. As it is an irreversible process, not considered for the $CO_2$ capture and release. Overall, these chemical transformations also do not help to mitigate global warming, as the energy consumed in different forms is much higher than the amount of $CO_2$ fixed by chemical reactions. Here we describe the development of re-generable chemical fixation of $CO_2$ by spiroaziridineoxindole, where $CO_2$ is captured (chemical fixation) under catalyst-free condition at room temperature both in aqueous and non-aqueous medium even directly from the slow stream of flue gas producing regioselectivelyspirooxazolidinyloxindoles, a potential drug. The $CO_2$-adduct is reversed back to the spiroaziridine releasing $CO_2$ under mild conditions. Further both the fixation-defixation of $CO_2$ can be repeated under near ambient conditions for several cycles in a single loop using a recyclable reagent.



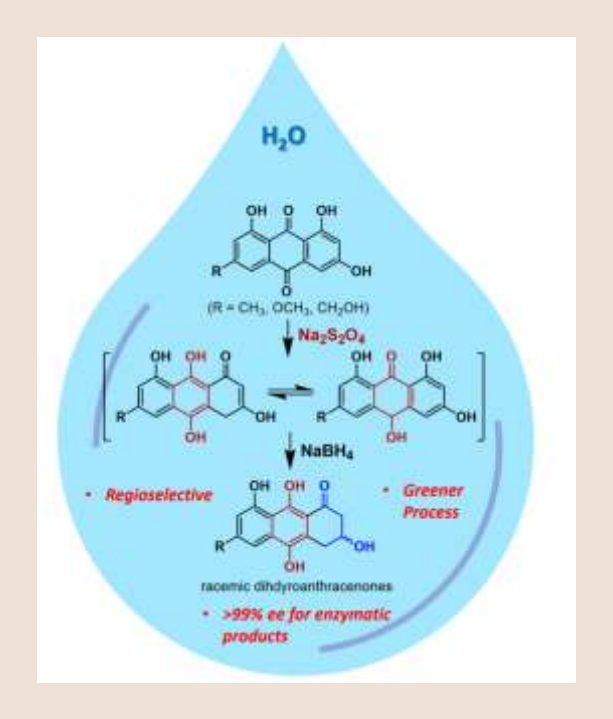

Chemical fixation-defixation cycles at 70 °C in a single vessel.

Schematic showing efficient chemical fixation and defixation cycle of carbon dioxide under ambient conditions

# A biomimetic synthesis of racemic dihydroanthracen-1(2*H*)-ones using sodium borohydride in water

Mondal A, Singh SK, Saha N and Husain SM
***European Journal of Organic Chemistry*** (2020), 16, 2425-2430

Herein, we have developed a general strategy for the synthesis of racemic dihydroanthracenones by the regioselective reduction of anthraquinones using $NaBH_4$ in the presence of $Na_2S_2O_4$ in water. Under the optimized conditions variously substituted racemic dihydroanthracenones were obtained in 42–60% yields. Racemic dihydroanthracenones were utilized for the determination of enantiomeric excess for the chemoenzymatically reduced (*R*)-configured dihydroanthracenones. Both MdpC of *Aspergillus nidulans* or PHAR of *Cochliobolus lunatus* catalyzes the stereoselective reduction of hydroanthraquinones with >99% ee.



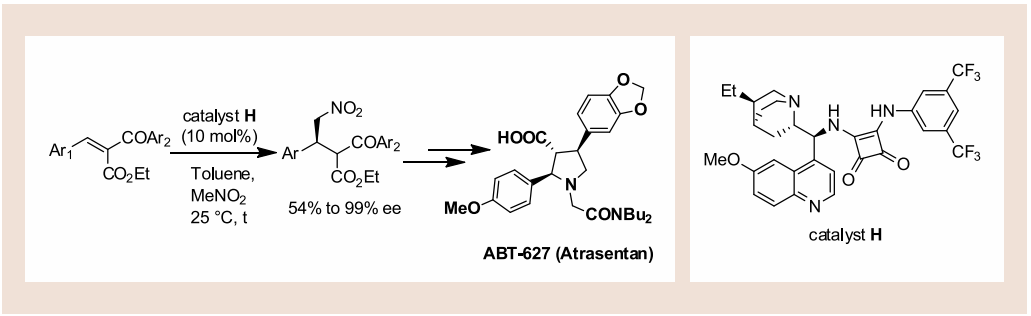

Schematic showing use of sodium borohydride in water for biomimetic synthesis of racemic dihydroanthracen-1(2H)-ones

# Organocatalytic enantioselective conjugate addition of nitromethane to benzylidene-2-benzoyl acetate: Asymmetric synthesis of ABT-627, an endothelin receptor antagonist

Hajra S, Aziz SM, Jana B and Hazra S
***Frontiers Chemistry***
(2020), 8, 135

The 2,4-disubstituted pyrrolidine-3-carboxylic acids are of particular interest owing to their preclinical and clinical activities towards endothelin-A receptor antagonists such as ABT 627 and ABT 546. Asymmetric synthesis of ABT 627 is an active research area.

Recently, first catalytic and enantioselective conjugate addition of nitromethane to benzylidene-2-benzoyl acetate has been developed using dihydroquinine derived squaramide catalyst with moderate to high selectivities. Asymmetric total synthesis of ABT-627, a potent ETA receptor antagonist is accomplished utilizing the developed method in overall 15.7% yield.




Asymmetric synthesis of ABT-627 following organocatalytic enantioselective conjugate addition of nitromethane to benzylidene-2-benzoyl acetate

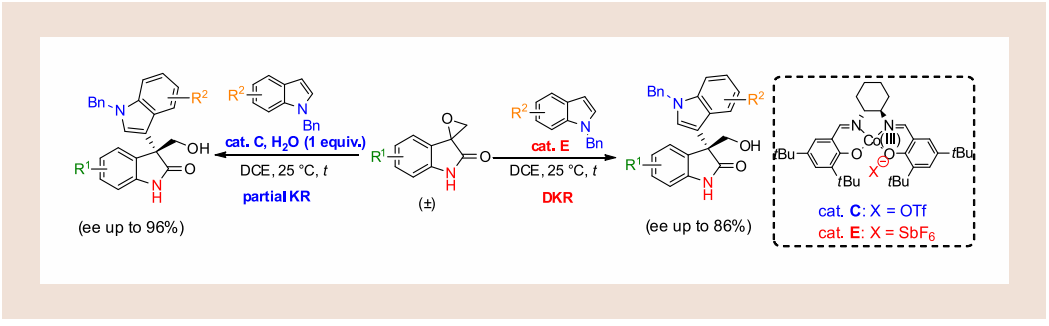
# Feedback inhibition in chemical catalysis leads dynamic kinetic to kinetic resolution in C3-indolylation of spiro-epoxyoxindoles

Molecules containing a quaternary stereocentre comprised 12% of the top 200 prescription drugs sold in 2011 and all these drugs are derived from naturally occurring compounds. Thus indole alkaloids containing quaternary stereocentre are attractive. Owing to their medicinal relevance and structural complexity, indole alkaloids is a fertile area of research worldwide. Thus the discovery and development of new chemical reactions for the efficient and scalable synthesis of targeted natural products with diversity is a great challenge. 3,3 -Bisindole, in particular, 3a-(3-indoyl)-hexahydropyrrolo[2,3-b]indole, is a unique structural skeleton present in and precursor to many indole alkaloids, which are endowed with remarkable biological and pharmacological activities.

Recently, we have originated a strategy for the chiral salen-Co(III) complex catalyzed C-3 indolylation of *N*-free spiro-epoxyoxindoles for the synthesis of highly enantioenriched 3-(3-indolyl) oxindole-3-methanols, a privileged building block for the synthesis of a large variety of 3,3′-bisindole alkaloids. The diverse substrate variation, the first ever generation of all carbon quaternary stereocentre from any kind of epoxide by implementing chiral salen-metal complex.

The first feedback inhibition, similar to enzyme catalysis, in Co(III)salen catalyzed asymmetric ring opening reaction of *N*-free spiro-epoxyoxyindole has been discovered, which leads dynamic kinetic to kinetic resolution. This is the first report of the enantioselective construction of all carbon quaternary center from any epoxide employing metal-salen catalyst till date. This protocol provides an easy access of 3-(3- indolyl)-oxindolemethanols, a privileged building block for the synthesis of a large variety of 3,3′-bisindole alkaloids.

Hajra S and Roy S
***Organic Letters*** (2020), 22, 1458-1463

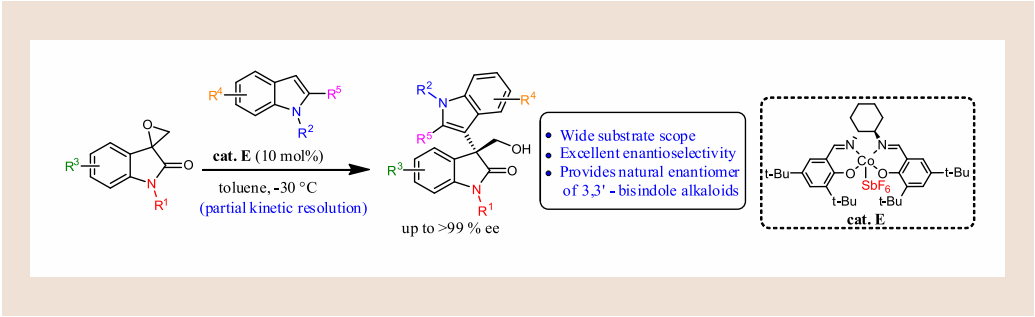



Example showing feedback inhibition in chemical catalysis causing dynamic kinetic to kinetic resolution in C3-indolylation of spiro-epoxyoxindoles

# Co(III)salen catalyzed enantioselective C3-indolylation of spiro-epoxyoxindoles and its mechanistic studies

Hajra S, Roy S and Mondal AS
***Advanced Synthesis and Catalysis*** (2020), 362, 5475-5484

3,3 -Bisindole, in particular, 3a-(3-indoyl)-hexahydropyrrolo[2,3-b]indole, is a unique structural skeleton present in and precursor to many indole alkaloids, which are endowed with remarkable biological and pharmacological activities.A catalytic asymmetric C3-indolylation of *N*-protected spiro-epoxyoxindoles has been developed for the access of 3-(3-indolyl)-oxindolemethanols with excellent enantioselectivity (ee up to >99%). The widespread substrate scope and easily accessible Co(III)-salen over SPINOL phosphoric acid prove our condition to be more beneficial than the chiral Brønsted acid-catalyzed reaction. Further, kinetic resolution of spiro-epoxides is achieved in high enantiomeric excess under certain conditions. The detailed mechanistic study endorses that the feedback inhibition played a key role which restricts the DKR process. Besides it also revealed the $S_N2$ mechanism for the Co(III)-salencatalysed C3-indolylation of spiro-epoxyoxindoles.

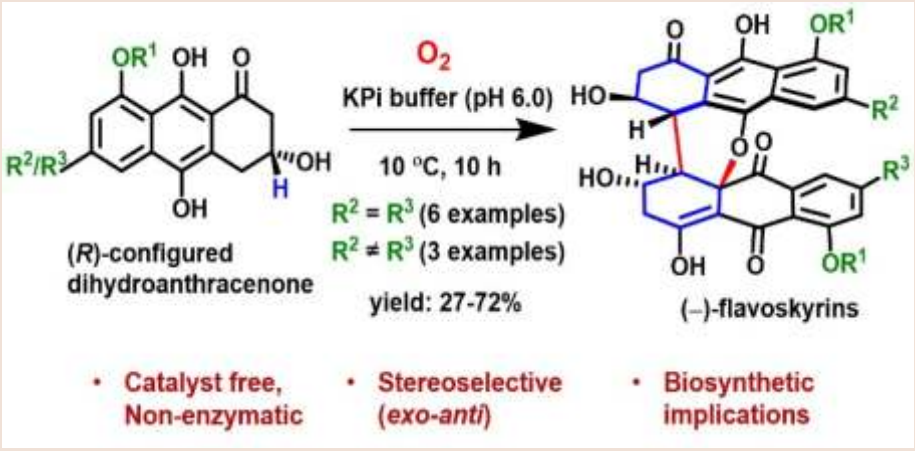



Enantioselective C3-indolylation of spiro-epoxyoxindoles using Co (III) salen catalysis

# Synthesis of (–)-flavoskyrins by catalyst free oxidation of (*R*)-configured dihydroanthracenones in aqueous media and its (bio) synthetic implications

A catalyst-free method for the synthesis of dimeric, (−)-flavoskyrins has been developed. It involves the autooxidation of chemoenzymatically synthesized, (*R*)-configured dihydroanthracenones in the presence of molecular oxygen in buffer of pH 6.0, followed by spontaneous [4 + 2] cycloaddition in stereocontrolled *exo*-anti fashion to form (−)-flavoskyrins. The method is applied to obtain several homo- as well as heterodimerized flavoskyrins (9 examples) in 27-72% yield and further implies the involvement of a similar pathway in the (bio)synthesis of modified bisanthraquinones and their analogs. The method is greener, biomimetic,and supports the role of non-enzymatic oxidation during flavoskyrins biosynthesis, as postulated for several natural products. The work also speculates the existence of diastereomeric flavoskyrins synthesized here as biosynthetic intermediates which may be isolated in the future.

Mondal A, De A and Husain SM
***Organic Letters*** (2020), 22, 8511-8515

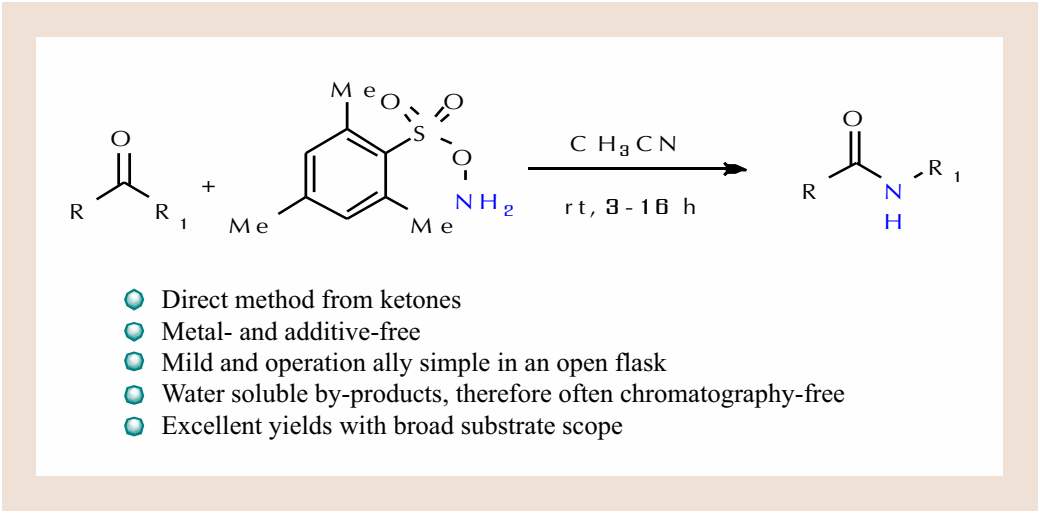



Catalyst free oxidation of (R)- configured dihydroanthracenones gives (−)-flavoskyrins

# Direct synthesis of secondary amides from ketones through Beckmann rearrangement using O-(mesitylsulfonyl) hydroxylamine

Chandra D, Verma S, Pandey CB, Yadav AK, Kumar P, Tiwari B and Jat JL
***Tetrahedron Letters*** (2020), 61, 151822

The Beckmann rearrangement is a versatile method for the preparation of secondary amides from ketones *via* oxime intermediates and has been widely used in the synthesis of bioactive natural products and pharmaceuticals. Herein, we have developed a highly efficient direct method for the preparation of secondary amides and lactams from ketones using *O*-(Mesitylsulfonyl)hydroxylamine (MSH). The reactions proceed rapidly at room temperature under mild condition without requiring any additive, and tolerate multiple functional groups. A simple aqueous work-up often furnished the products in excellent yield with high purity.

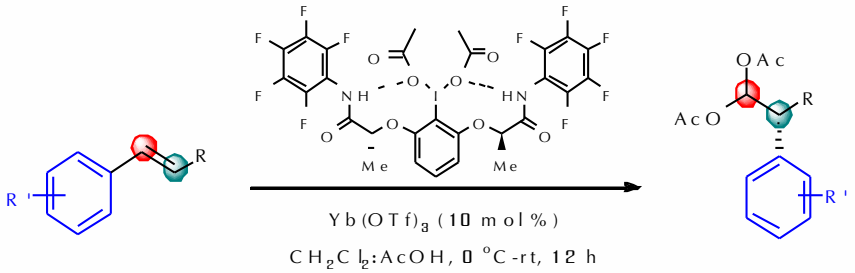



Secondary amides synthesized directory from ketones through Beckmann rearrangement using O-(mesitylsulfonyl) hydroxylamine

# Stereoselective oxidative rearrangement of di-substituted unactivated alkenes using hypervalent iodine(III) reagent

Pandey CB, Azaz T, Verma R, Mishra M, Jat JL and Tiwari B
***Journal of Organic Chemistry*** (2020), 85, 10175-10181

The stereoselective oxidative rearrangement of disubstituted unactivated olefins has been achieved using hypervalent iodine(III) reagent. The aryl group undergoes 1,2-migration to give *tert*-*α*-arylated aldehydes (as acetals). The preparation of these aldehydes/acetals, especially containing a *tert*-benzylic stereocentre, has remained challenging. This migration-based method provides a complementary approach over the known *α*-substitution-based methods for accessing this class of molecules.



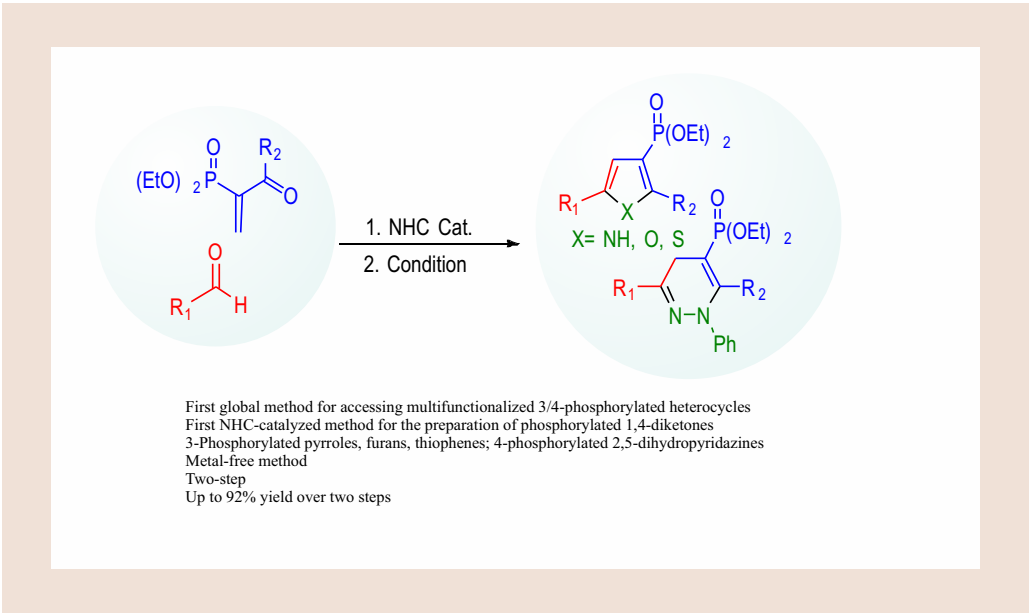

- First stereoselective rearrangement in disubstituted unactivated alkenes
- The challenging tert-a-arylated aldehydes (as acetals) were obtained
- A complementary approach via 1 ,2-migration of arylgroups
- A pentafluo roaniline-derived new hypervalent iodine was developed

Hypervalentiodine(III) reagent used for stereoselective oxidative rearrangement of di-substituted unactivated alkenes

# Global access to 3/4-phosphorylated heterocycles via a carbene-catalyzed stetter reaction of vinylphosphonates and aldehydes

Verma RS, Mishra M, Kumar S, Tiwari B
***Journal of Organic Chemistry*** (2020), 85, 8166-8169

The first global method for the preparation of 3-phosphorylated-pyrroles, furans, thiophenes, and 4-phosphorylated 2,5-dihydropyridazines is reported. To achieve this, the first protocol for the direct synthesis of $\alpha$-phosphorylated 1,4-diketones has been developed through a carbene-catalyzed Stetter reaction of vinylphosphonates and aldehydes. This is the first synthetic method for accessing 4-phosphorylated 2,5-dihydropyridazines. This process is metal-free and produces multi-functionalized heterocycles.

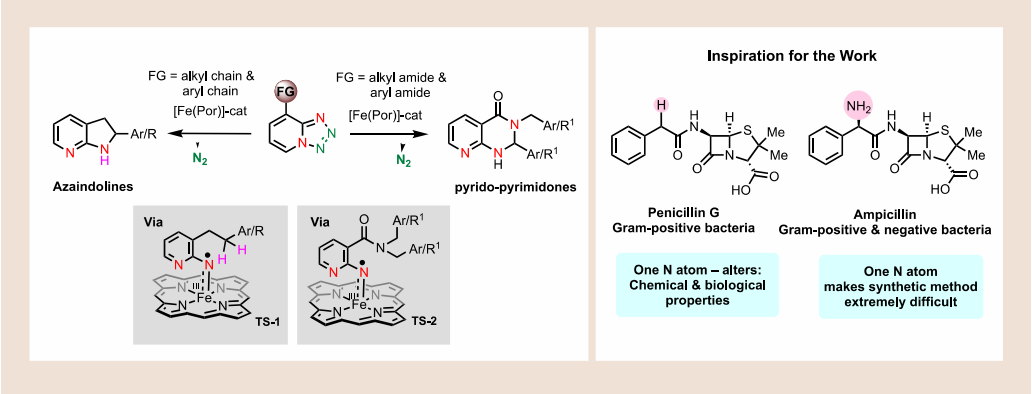



Synthesis of 3/4-phosphorylated heterocycles via a carbene-catalyzed stetter reaction of vinylphosphonates and aldehydes

# Iron-catalyzed amination of strong aliphatic C(sp$^3$)–H bonds

Das SK, Roy S. Khatua H and Chattopadhyay B
***Journal of the American Chemical Society*** (2020), 142, 16211-16217

A concept for intramolecular denitrogenative C(sp$^3$)–H amination of 1,2,3,4-tetrazoles bearing unactivated primary, secondary and tertiary C–H bonds is discovered. This catalytic amination follows an unprecedented metalloradical activation mechanism. The utility of the developed method is showcased with the short synthesis of a bioactive molecule. Moreover, an initial effort has been embarked for the enantioselective C(sp$^3$)–H amination through the catalyst design. Collectively, this study underlines the development of C(sp$^3$)–H bond functionalization chemistry that should find wide application in the context of drug discovery and natural product synthesis.

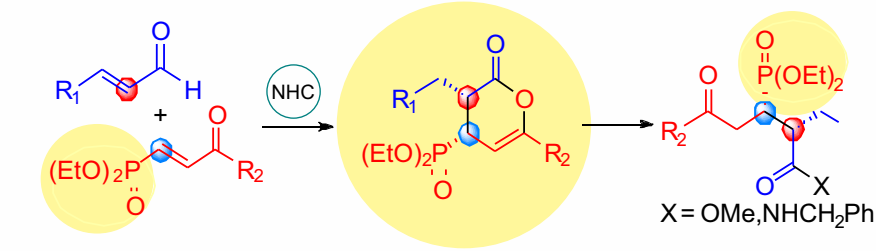



Schematic showing Iron-catalyzed amination of strong aliphatic C(sp$^3$)–H bonds

# Access to enantioenriched 4-phosphorylated δ-lactones from β-phosphorylenones and enals via carbene organocatalysis

Verma RS, Khatana AK, Mishra M, Kumar S and Tiwari B
***Chemical Communications***
(2020), 56, 7155-7158

The first N-Heterocyclic Carbene (NHC) catalyzed direct access to enantioenriched 4-phosphorylated *δ*-lactones from *β*-phosphorylenones and enals has been achieved. The sterically demanding *β*-phosphonate-substituted enones, having competing regiomeric reaction centres, have remained elusive so far in intermolecular cycloaddition reactions under NHC catalysis. All the products were obtained in excellent yield and enantioselectivity. These phosphorylated *δ*-lactones could be transformed to the challenging multi-functionalized chiral esters and amides loaded with *β*-ketophosphonate functionality.

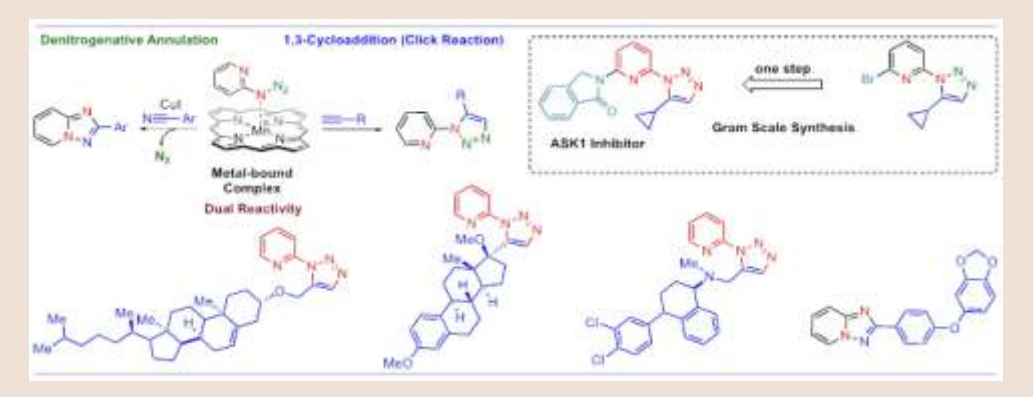



Carbene organocatalysis for the synthesis of enantioenriched 4-phosphorylated *δ*-lactones from β-phosphorylenones and enals

# Dual reactivity of 1,2,3,4-tetrazole: Manganese-catalyzed click reaction and denitrogenative annulation

Khatua H, Das SK, Roy S and Chattopadhyay B
***Angewandte Chemie International Edition***
(2021), 60, 304-312

A general catalytic method using Mn-porphyrin-based catalytic system is discovered that enables two different reactions (click reaction and denitrogenative annulation) affording two different classes of nitrogen heterocycles, such as 1,5-disubstituted 1,2,3-triazoles (with a pyridyl motif) and 1,2,4-triazolo-pyridines. Mechanistic investigations suggest that while click reaction likely proceeds through an ionic mechanism, which is different from the traditional click reaction, denitrogenative annulation undergoes likely via an electrophilic metallonitrene intermediate rather than the metalloradical intermediate. Collectively, the discovered method is highly efficient that offer obvious advantages over other methods, as it excludes multi-step synthesis of these classes of N-heterocyclic molecules and produces only environmentally benign $N_2$ gas by-product.

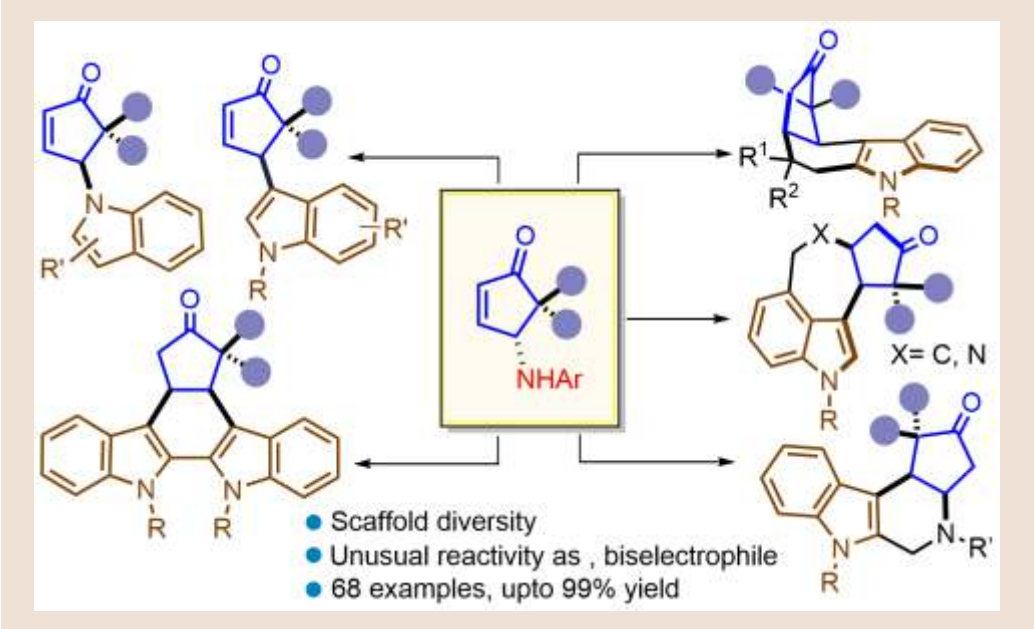



Manganese-catalyzed click reaction and denitrogenative annulation showing dual reactivity of 1,2,3,4-tetrazole

# Method development for the synthesis of diverse indole alkaloid-like compounds of biological relevance

Jagadeesh C, Mondal B, Pramanik S, Das D and Saha J ***Angewandte Chemie International Edition*** (2021), 60, 8808-8812

Observation of an unexpected, Lewis acid promoted displacement of latent reactive γ-amino group on cyclopentenone presented unparalleled opportunity for enone functionalization and annulations with indole derivatives, which is developed in the current study. Herein, a vast range of C3/N-indolyl enones and indole alkaloid-like compound were accessed in excellent yields (up to 99%) and selectivity through a one-pot operation. The mechanism most likely involves an unprecedented trait of Piancatelli-type rearrangement where influence of the gem-diaryl group appeared crucial.

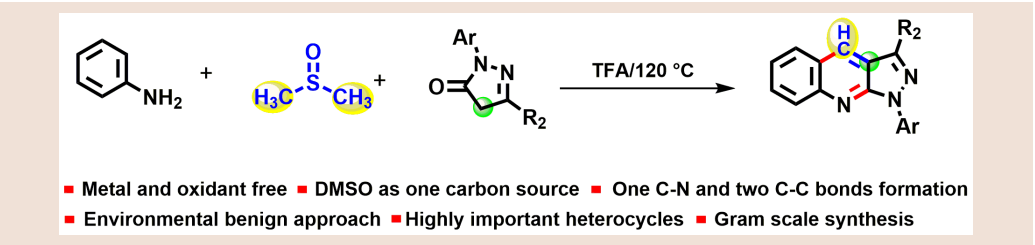



Diversity-oriented synthesis of functionalized indoles and indole-annulated ring structures using unprecedented reactivity of γ-amino cyclopentenone

# DMSO as a methine source in TFA-mediated one-pot tandem regioselective synthesis of 3-substituted-1-aryl-1H-pyrazolo-[3,4-b] quinolines from anilines and pyrazolones

Yadav P, Awasthi A, Gokulnath S and Tiwari DK
***Journal of Organic Chemistry*** (2021), 86, 2658-2666

Pyrazoloquinolines,including Pyrazolo[3,4-b]quinolinesare considered an important class of N-containing heterocycles frequently encountered in various natural products and pharmaceuticals that displays a wide range of biological activities such as antiviral, antimicrobial oncogenic Ras and to lowering of serum cholesterol, FLT3-mediated disorders, and anti-cancer activities.In addition, the pyrazolo[3,4-b]quinoline derivatives have found a great application in material chemistry as blue or green light emitters with electron-transporting properties. They are widely used as fluorescent molecular probe and electroluminescent materials.Owing to the wide range of applications of 3-substituted-1-aryl-1H-pyrazole-[3,4-b]quinolines we developed an efficient and mild approach for their synthesis. This reaction proceeds through in situ generations of imine/enamine followed by one carbon homologation and elimination to form azadiene which subsequently undergoes intramolecular cyclization reaction cascades in a single pot to access a wide range of 3-substituted-1-aryl-1H-pyrazole-[3,4-b]quinolines. Notably, the DMSO activation in pyrazolone is not known to date.

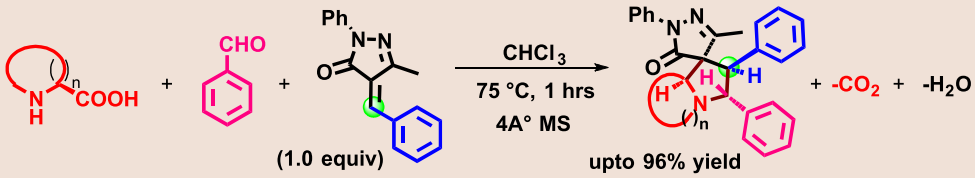



TFA-mediated one-pot tandem regioselective synthesis of 3-substituted-1-aryl-1h-pyrazolo-[3,4-b]quinolines from anilines and pyrazolones using DMSO as a methine source

# Three component, general and practical route for diastereoselective synthesis of aza-spirocyclic pyrazolones via decarboxylative annulation process

Awasthi A, Yadav P and Tiwari DK
*New Journal of Chemistry* (2021), 45, 2374-2383

Pyrazolones and its derivatives are an important class of heterocycles present in various biologically important molecules and drugs present in the market In addition, they found wide use in the field's functional materials, coordination chemistry, dyes and pigments. In the recent past, the spirocyclicpyrazolones have received a great attention from synthetic and medicinal chemists due to their frequent appearance in a large number of bioactive natural alkaloids and pharmaceutical agents associated with a numerous biological activities such as anti- bacterial, antidiabetic, analgesic, anti-inflammatory, PPAR α-antagonists, antiviral, anticancer, and type-4-phosphodiesterase inhibitor activities. In view of pharmaceutical importance of spirocyclicpyrazolones, we herein report a mild and efficient three component approach for the synthesis of highly functionalized aza-spirocyclicpyrazolones from readily available starting materials. This one pot tandem reaction proceeds through [3+2]-cycloaddition between alkylidinepyrazolones and azomethineylides, generated in situ from cyclic α-amino acids and aldehyde.




A three component approach for the synthesis of aza-spiropyrazolones

Diastereoselective synthesis of aza-spirocyclic pyrazolones via a decarboxylative annulation process (a three-component, general and practical route)

# Remarkably efficient iridium catalysts for directed C(sp2)-H and C(sp3)-H borylation of diverse classes of substrates

Here we describe the discovery of a new class of C–H borylation catalysts and their use for regioselective C–H borylation of aromatic, heteroaromatic, and aliphatic systems. The new catalysts have Ir–C(thienyl) or Ir–C(furyl) anionic ligands instead of the diamine-type neutral chelating ligands used in the standard C–H borylation conditions. It is reported that the employment of these newly discovered catalysts shows excellent reactivity and ortho-selectivity for diverse classes of aromatic substrates with high isolated yields. Moreover, the catalysts proved to be efficient for a wide number of aliphatic substrates for selective C(sp3)–H bond borylations. Heterocyclic molecules are selectively borylated using the inherently elevated reactivity of the C–H bonds. A number of late-stage C–H functionalization have been described using the same catalysts. Furthermore, we show that one of the catalysts could be used even in open air for the C(sp2)–H and C(sp3)–H borylations enabling the method more general. Preliminary mechanistic studies suggest that the active catalytic intermediate is the Ir(bis)boryl complex, and the attached ligand acts as bidentate ligand. Collectively, this study underlines the discovery of new class of C–H borylation catalysts that should find wide application in the context of C–H functionalization chemistry.

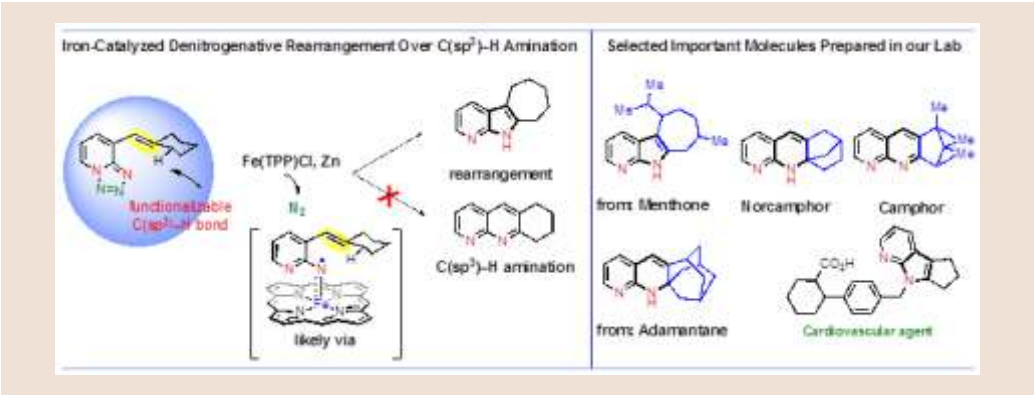
Hoque E, Hassan MMM and Chattopadhyay B
***Journal of the American Chemical Society*** (2021), 143, 5022–5037


Catalyst development for directed C-H activation and borylation

# Iron-catalyzed radical activation mechanism for denitrogenative rearrangement over C(sp3)–H amination

Roy S, Das SK, Khatua H, Das S, Singh KN and Chattopadhyay B
***Angewandte Chemie International Edition***
(2021), 60, 8772-8780

An iron-catalyzed denitrogenative rearrangement of 1,2,3,4-tetrazole is developed over the competitive C(sp3)–H amination. This catalytic rearrangement reaction follows an unprecedented metalloradical activation mechanism. Employing the developed method, a wide number of complex-N-heterocyclic product classes have been accessed. The synthetic utility of this radical activation method is showcased with the short synthesis of a bioactive molecule. Collectively, this discovery underlines the progress of radical activation strategy that should find wide application in the perspective of medicinal chemistry, drug discovery and natural product synthesis research.

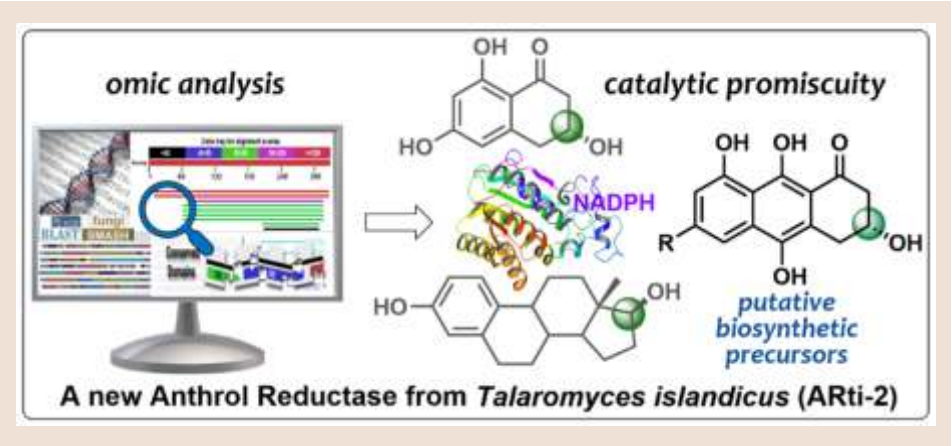



Denitrogenative rearrangement over C(sp3)–H amination using iron-catalyzed radical activation and its mechanism

# Promiscuity of an unrelated anthrol reductase of *talaromyces islandicus* WF-38-12

Singh SK, Rajput A, De A, Chakraborti T and Husain SM
***Catalysis Science & Technology*** (2021), 11, 474-478

An anthrol reductase of *Talaromyces islandicus* WF-38-12 (ARti-2) from an unrelated biosynthetic gene cluster (BGC) has been identified and characterized. It catalyzes the NADPH-dependent stereoselective reduction of anthrols (hydroanthraquinones), estrone, and a naphthol with high stereo- and regioselectivity. Also, we could determine the kinetic parameters of these enzymes using reversed-phase HPLC. Although the role of another associated gene, CRG89872.1, a putative anthraquinone reductase could not be verified, it might have a crucial role to play in the biosynthesis of (*R*)-configured dihydroanthracenones and other more complex dimeric bisnathraquinones. Considering the isolation of (-)-flavoskyrin and (-)-rugulosin from *T. islandicus*, we have proposed the role of CRG89872.1, ARti-2, and the non-enzymatic transformations in their biosynthesis.




A new anthrol reductase of *Talaromyces islandicus* is identified and characterized for its catalytic activity

# Research Output Indicators

## Research Publications (2020-2021)

| IF | 2020-21 |
|---|---|
| >15 | 06 |
| >10 | 01 |
| >5 | 21 |
| <5 | 44 |
| Total Papers | 72 |
| Average IF | 4.27 |

01. Hafis Muhammed, Dinesh Kumar, Durgesh Dubey, Sandeep Kumar, Smriti Chaurasia, Anupam Guleria, Sanjukta Majumder, Rajeev Singh, Vikas Agarwal and Ramnath Misra (2020). Metabolomics analysis revealed significantly higher synovial Phe/Tyr ratio in reactive arthritis and undifferentiated spondylo-arthropathy. ***Rheumatology***, 59 (7): 1587-1590.

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# Patents filed

| S.No. | Title | Inventors | Filing date | App. number | Country |
|---|---|---|---|---|---|
| 1. | Catalyst/ ligand engineering for C–H borylation of diverse classless of aromatic and heteroaromatic molecules | Hoque, E.; Hassan, M.; Chattopadhyay, B. | February 05, 2020 | 202011005091 | India |
| 2. | Method of manganese-catalyzed activation of 1,2,3,4-tetrazoles for nitrogen heterocycle synthesis via click and denitrogenative annulation | Khatua, H.; Das, S. K.; Roy, S.; Chattopadhyay, B. | May 23, 2020 | 202011021740 | India |
| 3. | Method of meta–selective borylation of aromatic molecules. | Chaturvedi, J.; Haldar, C.; Bisht, R.; Chattopadhyay, B. | August 20, 2020 | 202011035905 | India |
| 4. | Method for preparation of intermediates useful for preparation of eupalinilide E and analogs thereof | Hajra, S.; Maity, R. | July 13, 2021 | 202111031519 | India |
| 5. | Substituted methanopyrido[2,1a] isoindoles as mAChR modulators for treating various associated phthophyological conditions and process for preparation thereof | Pandey, G.; Varkhedkar, R.; Dogra, S.; Tiwari, D.; Hussain, Y.; Yadav, P. N. | July, 20, 2021 | 20200121657 | US |

# Ph.D. Awarded

| Name | Year | Supervisor | University | Title | Subject |
|---|---|---|---|---|---|
|  **Sayan Roy** | 2020 | Dr. Saumen Hajra, Professor | Banaras Hindu University (BHU), Varanasi | Investigation of the Unprecedented Reactivity of Spiro-epoxyoxindoles Towards the Synthesis of Indole Based Bio-active Molecules | Chemistry |
|  **Bibekananda Jana** | 2020 | Dr. Saumen Hajra, Professor | IIT Kharagpur | Organocatalytic Enantioselective Aza-Henry Reaction-Cyclization and Mukaiyama-Mannich Reactions of Ketimines: Synthetic Applications | Chemistry |
|  **Durgesh Dubey** | 2020 | Dr. Dinesh Kumar, Associate Professor | Babasaheb Bhimrao Ambedkar University (BBAU), Lucknow | NMR based Metabolomics of Synovial Fluid from patient with Reactive Arthritis (ReA) for Identifying abnormal metabolic status | Biotechnology |
|  **Manvendra Pratap Singh** | 2020 | Dr. Raja Roy, Professor | Integral University, Lucknow | Metabolomic Analysis of Saliva in Periodontitis and its Treatment Follow Up Study by NMR Spectroscopy | Life Sciences |
|  **Sreemoyee Chakraborti** | 2020 | Dr. Biswanath Maity, Assistant Professor | University of Kalyani | G Protein Dependent and Independent Regulation of Multiple Chemotherapeutics and Nsaids Induced Cardiotoxicity | Zoology |
|  **Md. Emdadul Hoque** | 2021 | Dr. Buddhadeb Chattopadhyay, Assistant Professor | Banaras Hindu University (BHU), Varanasi | Iridium-Catalyzed Proximal and Distal C-H Bond Activation and Borylation of Arenes | Chemistry |

| Name | Year | Supervisor | University | Title | Stream |
|---|---|---|---|---|---|
|  **Atanu Hazra** | 2021 | Dr. Saumen Hajra, Professor | Banaras Hindu University (BHU), Varanasi | Asymmetric Synthesis of 3,3-Disubstituted Oxindoles and SpirocyclicOxindoles | Chemistry |
|  **Satyajit** | 2021 | Dr. Buddhadeb Chattopadhyay, Assistant Professor | Banaras Hindu University (BHU), Varanasi | Denitrogenative Annulation of 1,2,3,4-Tetrazoles and 1,2,3-Triazoles: Converting Tetrazole and Triazole to Other Nitrogen Heterocycles | Chemistry |
|  **Anup Poul** | 2021 | Dr. Raja Roy, Professor | University of Lucknow, Lucknow | Nuclear magnetic resonance spectroscopy for biomedical application | Chemistry |
|  **Ajay Verma** | 2021 | Dr. Bikash Baishya, Associate Professor | Banaras Hindu University (BHU), Varanasi | Homo-Decoupling Methodology in Two-Dimensional NMR for Deciphering Overlapped Proton Signals in Biofluids and Complex Mixtures | Chemistry |

# Participation in Symposia/Conferences/ Workshops

| | | | | |
|---|---|---|---|---|
|  | **Dr. Neeraj Sinha**<br>**Professor** | Saurashtra University, Rajkot | 2020 | Invited talk - 26th National Magnetic Resonance Society Meeting & International Conference on NMR from "Molecules to Human Behavior and Beyond" |
|  | **Dr. Saumen Hajra**<br>**Professor** | IIT Kharagpur | 2020 | Invited talk - International Conference on "Emerging Trends in Catalysis & Synthesis (IC-ETCS) |
| | | IISER Kolkata | 2020 | Invited talk- 57th Annual Convention of Chemists (ACC) - Indian Chemical Society (ICS) Recent Trends in Chemical Sciences |
|  | **Dr. Bhoopendra Tiwari**<br>**Associate Professor** | CSIR-IMMT, Bhubaneshwar | 2020 | International Conference on Global Challenges in Nanomaterial Research for Environmental and Healthcare Applications |
|  | **Dr. Dinesh Kumar**<br>**Associate Professor** | Saurashtra University, Rajkot | 2020 | Invited talk - 26th National Magnetic Resonance Society Meeting & International Conference on NMR from "Molecules to Human Behavior and Beyond" |
| | | Institute of Science, Banaras Hindu University, Varanasi | 2020 | Invited lecture "8th International Translational Cancer Research Conference: Role of Inflammation and Immune System for Cancer Prevention and Treatment" Organized in association with Society for Translational Cancer Research (STCR). |
| | | Shri Ramswaroop Memorial University (SRMU), Lucknow | 2020 | Invited talk in POPULAR LECTURES IN BIOTECHNOLOGY (Sponsored by DBT –CTEP, Ministry of Science and Technology Government of India) |
| | | ICAR-National Dairy Research Institute (NDRI), Karnal | 2020 | Delivered lectures in the National Workshop on "Metabolomics: Basic principles and Applications" under Institutional Development Plan (IDP)-National Agricultural Higher Education Project (NAHEP) |

**Dr. Buddhadeb Chattopadhyay, Assistant Professor**

| | | |
|---|---|---|
| New York University, USA | 2021 | Invited Talk: New York University, Department of Chemistry. |
| Goa | 2020 | Invited Talk: ICOC-2020 Conference |
| Berhampur University, Odisha | 2020 | Invited Talk: National Organic Synthesis Conference (N-COS-2020) |

# Extramural Research Funding

| S. No. | Title | Sponsor | Principal Investigator | Sanction Year | Total Value (INR) |
|---|---|---|---|---|---|
| 1. | Asymmetric total synthesis of anticancer compounds – 3-O-(-D-glucopyranosyl) desoxypodophyllotoxin, propolisbenzofuran B and More | SERB | Prof. Saumen Hajra | 2020 | 63,33,292.00 |
| 2. | Tactile perceptual processing performance of deaf and hearing age groups functional magnetic resonance imaging fMRI study | DST | Dr. Uttam Kumar | 2020 | 59,61,240.00 |
| 3. | Investigation on the expansion of application portfolio of oxyallyl cation and related species from molecular synthesis to site-selective protein modification | SERB | Dr. Jaideep Saha | 2020 | 49,93,920.00 |
| 4. | Atypical G protein regulator Gβ5 might be developed as novel target to attenuate chemotherapeutics induced hypertrophy to heart failure transition CAMKII dependent T-tubule remodeling | DBT | Dr. Biswanath Maity | 2020 | 67,35,440.00 |
| 5. | C-H Borylation via attractive weak interaction | SERB | Dr. Buddhadeb Chattopadhyay | 2020 | 38,50,000.00 |
| 6. | Concept of catalyst engineering for borylation of small organic molecules | SERB | Dr. Buddhadeb Chattopadhyay | 2020 | 77,35,720.00 |
| 7. | Transition metal free one-pot tandem synthesis of medicinally relevant N-heterocycles using DMSO as carbon source | SERB | Dr. Dharmendra Tiwari | 2020 | 44,52,815.00 |
| 8. | Asymmetric total synthesis of eupalinilide E and allied guaianolides | CSIR | Prof. Saumen Hajra | 2021 | 33,92,000.00 |
| 9. | Analogue of prothrombin time: identification and assay development of novel non-invasive and surrogate indicator of blood coagulopathy | ICMR | Dr. Ashish Gupta | 2021 | 39,65,601.00 |
| 10. | Chemoenzymatic, asymmetric, Total synthesis of nodulones and their non-natural analogs using a fungal oxidoreductase enzyme and its biosynthetic implications | CSIR | Dr. Syed Masood Husain | 2021 | 31,42,000.00 |
| 11. | Exploring dual activation strategies using transient azaoxyallyl cations: New opportunity for heterocycle synthesis | CSIR | Dr. Jaideep Saha | 2021 | 29,60,000.00 |
| 12. | Metalloradical activation of 1,2,3,4-tetrazoles: New paradigm for nitrogen heterocycles | CSIR | Dr. Buddhadeb Chattopadhyay | 2021 | 23,00,000.00 |

# Recognitions

**Dr. Saumen Hajra**
Professor

- Member, SERB PAC-Organic Chemistry (2021-2024)
- Member, SGPGIMS Research Committee (2019-2022)

**Dr. Buddhadeb Chattopadhyay**
Assistant Professor

- SERB-Star Award – 2019
  (Awarded in 2020)

**Dr. Dinesh Kumar**
Associate Professor

- Elected Associate, Indian Academy of Sciences (2020-2022)

**Dr. Sayan Roy**
CSIR-SRF

- SAILIFE-NOST Best Thesis Award - 2020

# Sophisticated Instrument Facilities

## High Field NMR

CBMR houses state-of-the-art NMR spectrometers including 400 MHz (solution state), 600 MHz (for solid state) and 800 MHz (AVANCE III equipped with Cryoprobe, solution state NMR and high-resolution magic angle spinning (HRMAS) NMR for tissue samples).


Bruker 400 MHz NMR Spectrometer for routine solution state NMR experiments


Bruker 600 MHz NMR Spectrometer for Solid state NMR of biological solid materials

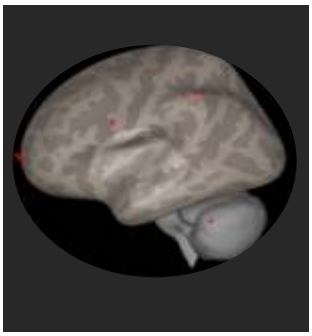

High field 800 MHz NMR Spectrometer for Solution state NMR and metabolomics studies.

Nuclear magnetic resonance (NMR) spectroscopy is considered as a master spectroscopy technique and has played a pivotal role in solving various problems in physics, chemistry, biology, biomedical, pharmaceutical, forensic, and health sciences. Over the years, NMR has evolved rapidly to study a wide array of topics related to biomolecular structure, dynamics, and function. Proteins, nucleic acids, lipids, polysaccharides, and other biomolecules and their complexes can be studied in solution or solid state sample conditions. The technological and methodological advancements in the area of NMR have made it a very powerful tool for studying the mechanistic structural biology of proteins and further to guide the rational drug discovery endeavors allowing (a) three-dimensional (3D) structure determination of proteins and other biological macromolecules, (b) screening of functional protein-protein, protein-nucleic acid or protein-ligand interactions, (c) characterization of their dynamics features at atomic level, all critically important to understand "how do these proteins function and how can their activity be altered?". The ability of NMR to study the molecular interactions, even in the case of weak affinity, opens up powerful opportunities for the development of pharmacologically active molecules. About 30% of the human proteome contains intrinsically disordered proteins (IDPs) and solution state NMR is the only technique for characterizing conformational and dynamics features of these IDPs and further their interaction with their physiological binding partners. Advances in magic-angle spinning solid-state NMR allow to study in detail peptide/protein aggregates and amyloids, protein complexes, membrane associated proteins, intact viruses, viral proteins, molecular assemblies (such as gelators, hydrogels, polymers etc.), and more. Such NMR studies are often combined with advanced computational approaches (such as molecular dynamics simulations) and integrated with other structural biology techniques such as X-ray crystallography and cryo electron microscopy. Continuous progress in hardware development, sample preparation techniques and integrated approaches facilitate the study of variety of biological systems with ever growing sophistication at unprecedented resolution. Together with X-ray crystallography, NMR spectroscopy is one of the two leading technologies for the structural determination of at atomic resolution.

# 3 Tesla fMRI

Research facilities offer the use of a state-of-the-art high-field MRI scanner (3T Siemens Magnetom Skyra) for structural and functional MRI (fMRI). This MRI scanner can be used for (clinical) diagnostics as well as fundamental or applied research. All body parts can be visualized in 3D or even 4D (3D in time). Dedicated coils are available for various body parts. The functional MRI facility is a core resource serving the research program. The facility provides a complete environment for stimulus presentation, monitoring and recording subject behavior and physiology while performing functional MRI.





# Glove Box

Glovebox is a sealed container that allows one to carryout the chemical reactions under a control atmosphere as desired. Built into sides are gloves arranged in such a way that the user can place their hands into the gloves and perform tasks inside the box without breaking containment. Part or all of the box is usually transparent to allow the user to see what is being manipulated. The glove box is used to carryout sensitive reaction.


# Protein Expression and Purification Facility

Laminar flow unit for microbiology and bacterial culture

Sonicator for processing bacterial cell pellet

Fast Protein Liquid Chromatography (FPLC) for purifying recombinant proteins for elucidating their structures and studying their interactions using NMR.

Orbital shaker for growing bacterial cultures

# Chemical Biology Facility

Gel Documentation System for visualization of DNA gels, image capturing and analyzing

PCR machine for qualitative and quantitative estimation of nucleic acids in biological samples in addition to regular genome enhancing and DNA cloning related work

Cooling centrifuge for routine experiments related to molecular cell biology, chemical biology, proteomics and metabolomics

# Advanced Chemistry Labs

Excellent infrastructure for modern molecular synthesis and drug discovery

Research facilities with state-of-the-art instruments and equipment

Strong pool of young innovative people, pursuing research in advance molecular synthesis

# Molecular Spectrometry

HR-MS: High Resolution Mass Spectrometry

GC-MS: Gas Chromatography-Mass Spectrometry

HPLC: High Performance Liquid Chromatography

GC-MS: Gas Chromatography-Mass Spectrometry

# Events

## National Symposium on Integrative Medicine and Health: From Basic to Translational Research

### December 4-6, 2020

The emergence of COVID-19 pandemic has imposed an unwavering commitment – from the scientific community – to harness all knowledge systems available globally to combat such dreadful pandemics in future. India has a rich heritage of traditional medicine systems such as Ayurveda, Unani, Siddha, and Homeopathy. However, the mechanistic understanding about the biological activity of majority of these formulations is still lacking to reinforce their integration with modern care systems. Further, the safety and efficacy data in addition to dose and quality parameters for majority of these traditional medicines is far from sufficient to meet the criteria needed to support their world-wide use as a pharmaceutical or nutraceutical product. Therefore, it is important to establish the scientific rationale for their world-wide therapeutic use, especially in the management of critical illnesses. For this, there is an unmet need of interdisciplinary collaborations between the biomedical scientists, clinical researchers and healthcare practitioners to create scientific evidence for integrative use of traditional and modern care systems. This symposium paved a way towards this noble objective of social impact.

The symposium served as an interdisciplinary platform for biomedical scientists, academic/clinical researchers, and healthcare practitioners to present and discuss their thoughts and ideas about integrating natural healthcare systems with evidence-based allopathic modern medicines. The approach –commonly known as integrative medication- has the potential to significantly improve the quality of life, especially of patients suffering from various intractable and chronic clinical conditions such as cancer, diabetes, neurological, respiratory, cardiovascular, and autoimmune diseases. The symposium further served as a platform for undergraduate and graduate students to interact with biomedical scientists, medical doctors and clinical researchers and exposed them to the recent developments in the field of alternative and complimentary medicines and their commercial aspects.

# Road Safety Awareness Drive

## January 18- February 17, 2021

Road safety awareness drive was performed as a part of the "National Road Safety Month" observed from 18th January-17th February 2021 as decided by The Ministry of Road Transport & Highways and Government of Uttar Pradesh.

The students of Class XII from Kendriya Vidyalaya SGPGIMS, Lucknow were invited to CBMR and made aware about various road safety measures including do not run on roads, never cross road at bends, always use the pedestrian crossing for walking across road, always wear a helmet for safe two wheeler riding, maintain awareness of traffic rules, understand traffic signals (Red: Stop, Yellow: Look, Green: Cross the road), always use sidewalks/footpaths while walking, and most important pay attention to vehicular movement around you. The activity helped reinforce the idea that road safety is important to secure people's life while on road and that we should not disobey the rules of the road. Indeed, school students can bring about a major change in the society if the awareness of such social issues is inculcated in them, as they can share the information with their parents, relatives and friends and drive such campaigns further.


CBMR students and faculty members performing road safety drive at Raebareli Road, Lucknow


Students of Class XII from Kendriya Vidyalaya, SGPGIMS, Lucknow during their visit to CBMR as a part of Road Safety Awareness Drive

# Visit of Kendriya Vidyalaya students to CBMR

## January 30, 2021

National Education Policy (NEP) of India has placed a lot of emphasis on promoting fundamental science and innovation which will serve as a strong foundation for Atmanirbhar Bharat with Aatmvishvaas. Therefore, to inculcate scientific temperament in students and further to inspire young generation to pursue a career in science, the Centre of BioMedical Research (CBMR), Lucknow initiated an awareness program for pupils from class VIII to XII. Progressing in this direction, CBMR on 30th January 2021 organized Science Awareness Day by inviting the students of Class-XII from Kendriya Vidyalaya, SGPGIMS, Lucknow. The students visited different labs such as molecular synthesis, cell culture and chemical biology labs at CBMR. They were also exposed to the functioning of various sophisticated instruments such as 3T MRI scanner, high field NMR spectrometers, GC-MS, LC-MS, etc. CBMR faculty's helped them to understand the basis of biomedical research and how this helps in the development of medicines (such as anti-cancer, anti-microbial and anti-viral) and diagnostic tests. It is proposed that CBMR will invite 8-10 students to pursue research during their summer vacation. The students were excited to see the labs and equipment which they have studied in textbooks. Overall, this activity helped reinforce the idea that the Atmanirbhar Bharat Abhiyan (or Self-reliant India Mission)– which is now the dream of every Indian- cannot be imagined without considering science in our daily life.


Professor Alok Dhawan, Director CBMR addressing the students of Kendriya Vidyalaya

Students of Class XII from Kendriya Vidyalaya during their visit to CBMR, Lucknow

# National Science Day

## February 28, 2021

CBMR hosted a virtual event on February 28, 2021 to celebrate National Science Day with the objective of commemorating the first Nobel prize in Science won by an Indian- Sir C.V. Raman for the discovery of the Raman effect. It is also celebrated to emphasize the culture of science and the application of science for the welfare of people. The theme for this year's National Science Day was 'Future of STI: Impact on Education Skills and Work' where STI stands for Science Technology and Innovation.

Professor Alok Dhawan, Director CBMR presented his opening remarks and welcomed all the participants. Professor Jayesh Bellare, Institute Chair Professor of Chemical Engineering at the Indian Institute of Technology, Bombay delivered a lecture on "The Materials Sciencemystery of Homeopathic and Ayurvedic Medicines solved through Nanotechnology". Professor Bellare shared his experience working on different medicine systems ranging from allopathic (doctor-driven), Ayurvedic bhasmas (Vaidya driven) to homeopathic remedies (patient driven). Ayurvedic bhasmas are unique metallic/mineral formulations prepared through grinding, heating and then quenching a variety of base materials). He explained how preparation of Ayurvedic bhasmas overlap with those of modern nanotechnology preparation methods. Therefore, scientific tools and techniques used routinely in advance nanoscience and nanotechnology labs can be explored for characterization of Ayurvedic bhasmas. Professor Bellare exquisitely explained how manufacturing of homeopathic remedies (prepared by a process of serial dilution of 1:100 per step) mimic the froth floatation induced by succession method and thus rendering the presence of active ingredients in these medicines even after extreme dilutions. He also provided rationale for the efficacy of majority of homeopathic medicines based on hormetic effect (biphasic effect) i.e., a substance that causes an inhibitory effect at high concentrations may have a medicinal (stimulating) effect at low concentration. The post-lecture session involved the discussion on the New Education Policy (NEP) of India which has now placed a lot of emphasis on promoting fundamental science and innovation which will serve as a strong foundation for Atmanirbhar Bharat with Aatmvishvaas.

# Faculty interaction between CBMR and SGPGIMS, Lucknow

## March 13, 2021

Faculty of CBMR made presentations pertaining to clinical metabolomics studies using NMR as well as translational research being done on 3T fMRI. This was attended by faculty of SGPGIMS, Lucknow and the subsequent interactions were fruitful in opening up new avenues of collaborative research.

Professor Alok Dhawan
Director, CBMR

Dr. Uttam Kumar
Additional Professor, CBMR

Dr. Ashish Gupta
Additional Professor, CBMR

Dr. Bikash Baishya
Associate Professor, CBMR

Dr. Dinesh Kumar
Associate Professor, CBMR

Dr. Biswanath Maity
Associate Professor, CBMR

Professor Sunil Kumar
Head, Department of Radiodiagnosis, SGPGIMS, Lucknow

Professor Swasti Tiwari
Head, Department of Molecular Medicine, SGPGIMS, Lucknow

Dr. Gaurav Pande
Additional Professor
Department of Gastroenterology
SGPGIMS, Lucknow

Dr. Dheeraj Khetan
Additional Professor
Department of Transfusion Medicine SGPGIMS, Lucknow

Dr. Amit K. Keshri
Additional Professor
Department of Neuro-otology
SGPGIMS, Lucknow

Dr. Durga P. Misra
Associate Professor
Department of Clinical Immunology & Rheumatology, SGPGIMS, Lucknow

# National Technology Day

## May 11, 2021

National Technology Day-2021 was commemorated at Centre of Biomedical Research (CBMR) on May 11, 2021 on a virtual platform to mark the achievements and contributions of our countrymen in the field of science and technology. The theme for this year's National Technology Day was "Science and Technology for a Sustainable Future". On this occasion, Professor Rohit Srivastava, Head, Department of Biosciences and Bioengineering, Indian Institute of Technology, Bombay (IIT-B) delivered a lecture on "Affordable Healthcare for India".

The lecture was attended by the faculty members and research scholars of the Centre. During his lecture, Professor Srivastava shared his experience of translating the basic lab discoveries into affordable medical devices. He demonstrated how basic fundamental science backed innovative technologies can help common man in getting affordable diagnostics and therapeutics. This included affordable technologies for blood chemistry, bio-absorbable bone screws, biodegradable sponges for wounds, micro needle patch and pump for transdermal drug delivery. Further, he emphasized on promoting interdisciplinary collaborations among medical doctors, clinical researchers, biomedical scientists and engineers for translating fundamental scientific and technological discoveries into innovative devices for the benefit of society. Overall, the activity reinforced for the researchers the idea that Atmanirbhar Bharat Abhiyan (Self-reliant India Mission) – which is now the dream of every Indian - cannot be imagined without bringing science and technology together to serve the humanity. Pursuing efforts in this direction, it has been decided that school pupils and graduate/post students will be invited at CBMR for inculcating scientific temperament and inspiring the young generation to pursue a career in science.

# World Environment Day

## June 05, 2021

World Environment Day is considered one of the most remarkable days for environmental action and is celebrated on June 5 every year across the globe. To focus on the importance of the environment and to remind everyone that the environment should not be taken for granted Centre of BioMedical Research (CBMR) celebrated the World Environmental Day on June 5, 2021 with this year's theme 'Ecosystem Restoration. The term 'Ecosystem Restoration' means to assist in ecosystems' recovery, which have been degraded by deforestation, pollution, and other human activities. Recovery can also be promoted by taking measures to conserve the ecosystem which is still intact. The ongoing pandemic has reminded us of the harm we have caused to Mother Earth and how essential it is to protect the environment.

Centre of BioMedical Research (CBMR) and Uttar Pradesh Academy of Sciences (UPAS) jointly hosted a live webinar on the occasion of World Environment Day on June 5, 2021. Professor Alok Dhawan, Director CBMR welcomed all the participants and Dr. C.M. Nautiyal, Secretary, UPAS presented the opening remarks and introduced Padma Bhushan Professor Padmanabhan Balaram, an Indian biochemist and a former director of the Indian Institute of Science in Bangalore. Professor Balaram delivered a very insightful lecture on the topic "Nature as Viewed Through the Lens of Chemistry and Biology". Dr P.K. Seth, NASI Senior Scientist Platinum Jubilee Fellow and Former CEO, Biotech Park, Lucknow presided over the function. Professor Sandeep Verma, Secretary SERB also shared his thoughts. The programme concluded with a vote of thanks from Professor Neeraj Sinha, Dean, CBMR.

Professor P. Balaram


Professor Alok Dhawan, CBMR

Professor P.K. Seth


Dr Chandra Mohan Nautiyal

Professor Sandeep Verma, SERB

Dr Poonam Kakkar

# अन्तर्राष्ट्रीय योग दिवस 2021
# International Day of Yoga 2021






# Governing Council/General Body

## Chairman

**Shri Rajendra Kumar Tiwari**
Chief Secretary
Government of Uttar Pradesh

## Vice Chairman

**Dr. Sanjeev Misra**
Director
All India Institute of Medical Sciences
Jodhpur

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**Dr. C.M. Gupta**
Chairman
Scientific Advisory Committee (SAC)

**Professor Jayesh Bellare**
Institute Chair Professor
Indian Institute of Technology-Bombay
Mumbai

**Dr. Sanjay Singh**
CEO
Gennova Biopharmaceuticals Ltd.
Pune

**Shri Anupam Jalote**
CEO
iCreate
Ahmedabad

**Smt. S. Radha Chauhan**
Additional Chief Secretary
Finance Department
Government of Uttar Pradesh

**Shri Alok Kumar**
Principal Secretary
Medical Education Department
Government of Uttar Pradesh

**Dr. Shekhar C. Mande**
Director General
Council of Scientific & Industrial Research
New Delhi

**Professor Ashutosh Sharma**
Secretary
Department of Science & Technology
New Delhi

**Dr. Renu Swarup**
Secretary
Department of Biotechnology
New Delhi

**Professor Balram Bhargava**
Director General
Indian Council of Medical Research
New Delhi

**Professor A.K. Singh**
Vice Chancellor
Atal Bihari Vajpayee Medical University
Lucknow

**Professor R.K. Dhiman**
Director
Sanjay Gandhi Postgraduate Institute of Medical Sciences
Lucknow

**Professor Alok Dhawan**
Director
Centre of BioMedical Research
Lucknow

Administrative Officer of Centre of BioMedical Research shall be the Non-Member Secretary of the Council.

# Scientific Advisory Committee

## Chairman

**Dr. C.M. Gupta**
Distinguished Professor
Institute of Bioinformatics and Applied Biotechnology
Bengaluru

## Members

**Professor Priya Abraham**
Director
ICMR-National Institute of Virology
Pune

**Dr. Rakesh K. Mishra**
Director
Tata Institute for Genetics and Society
Bengaluru

**Dr. Anurag Agrawal**
Director
CSIR-Institute of Genomics and Integrative Biology
New Delhi

**Dr. Rohit Srivastava**
Head and Professor
Department of Biosciences and Bioengineering
Indian Institute of Technology Bombay
Powai, Mumbai

**Professor Ramakrishna Vijayacharya Hosur**
Senior Professor
Department of Chemical Sciences
Tata Institute of Fundamental Research (TIFR), Mumbai

## Member Secretary

**Professor Alok Dhawan**
Director
Centre of BioMedical Research
Lucknow

# Finance Committee

## Chairman

**Professor Alok Dhawan**
Director
Centre of BioMedical Research
Lucknow

## Members

**Smt. S. Radha Chauhan**
Additional Chief Secretary
Finance Department
Government of Uttar Pradesh

**Shri Alok Kumar**
Principal Secretary
Medical Education Department
Government of Uttar Pradesh

**Dr. Neeraj Sinha**
Professor
Centre of BioMedical Research
Lucknow

**Dr. Uttam Kumar**
Additional Professor
Centre of BioMedical Research
Lucknow

## Member Secretary

**Shri Pankaj Sharma**
Finance Controller
Centre of BioMedical Research
Lucknow

# Sexual Harassment Complaint Committee

## Chairperson

**Dr. Vinita Prakash**
Principal
Isabella Thoburn College
Lucknow

## Members

**Professor Neeraj Sinha**
Dean
Centre of BioMedical Research
Lucknow

**Dr. Alka Shukla**
Medical Consultant
Centre of BioMedical Research
Lucknow

**Ms. Deepa Bakshi**
Assistant Accountant
Centre of BioMedical Research
Lucknow

# Right to Information Act-2005

**Professor Neeraj Sinha**
Dean
Centre of BioMedical Research
Lucknow

First Appellate Authority

**Dr. Uttam Kumar**
Additional Professor
Centre of BioMedical Research
Lucknow

Public Information Officer

# Institutional Human Ethics Committee

**(Constituted in accordance with ICMR norms w.e.f. July 1, 2021)**

## Chairman

**Dr. V.P. Kamboj**
Former Director
CSIR-Central Drugh Research Institute
Lucknow

## Members

### Clinicians

**Professor U.K. Mishra**
Former Head
Department of Neurology,
Sanjay Gandhi Postgraduate Institute of Medical Sciences
Lucknow

**Dr. Akash Agarwal**
Additional Professor
Department of Surgical Oncology,
Ram Manohar Lohia Institute of Medical Sciences
Lucknow

**Dr. Shubha Phadke**
Professor & Head
Department of Medical Genetics,
Sanjay Gandhi Postgraduate Institute of Medical Sciences
Lucknow

### Statistician

**Dr. Sheela Misra**
Professor
Department of Statistics
University of Lucknow
Lucknow

### Lay Person

**Shri Vimal Shukla**
Secretary
Meghdoot Gramodyog Sewa Sansthan
Lucknow

### Basic Medical Scientists

**Professor Abbas Ali Mahdi**
Head
Department of Biochemistry,
King George's Medical University
Lucknow

**Dr. Poonam Kakkar**
Former Chief Scientist
CSIR-Indian Institute Of Toxicology Research
Lucknow

**Dr. Alok Kumar**
Department of Molecular Medicine & Biotechnology
Sanjay Gandhi Postgraduate Institute of Medical Sciences
Lucknow

### Legal Expert

**Shri S. C. Verma**
Justice (Retd.), High Court, Allahabad
14/8 Metro City, Nishatganj
Lucknow

### Social Scientist/ Philosopher/ Ethicist/ Theologian

**Ms. Shachi Singh**
Founder and General Secretary
Ehsaas Foundation
Lucknow

## Member Secretary

**Professor Neeraj Sinha**
Dean
Centre of BioMedical Research
Lucknow

# Faculty

Professor Alok Dhawan
Director

Professor Neeraj Sinha
Dean

Professor Saumen Hajra

Dr. Uttam Kumar

Dr. Ashish Kumar

Dr. Bikash Baishya

Dr. Syed Masood Husain

Dr. Bhoopendra Tiwari

Dr. Dinesh Kumar

Dr. B. Chattopadhayay

Dr. Jaideep Saha

Dr. Biswanath Maity

Dr. Dharmendra Tiwari

# Staff


Mr. Pankaj Sharma


Mr. Amar Dixit


Mr. Ranbir Singh


Mr. Prashant Singh Shakya


Dr. Sumit Kumar Verma


Mr. Urfi Ahmad


Mr. Shyam Singh Chauhan


Mrs. Deepa Bakshi


Mr. Pradeep Kumar Dwivedi


Mr. Sachin Masih


Mr. Vikram Singh


Mr. Arun Kumar Singh


Mr. Suveb

# Research Scholars and Project Fellows

Abhishek Singh Sengar

Amit Mondal

Ananda Shankar Mondal

Annapurna Awasthi

Anshita Singh

Anshul Rajput

Arijit De

Bal Krishna Mishra

Bandana Singh

Biplab Mondal

Biswajit Sen

Ch. Jagadeesh


Dr. Ahamd Raza Khan


Dr. Alok K. Singh


Dr. Deepak Kumar


Dr. Pramod Kumar


Dr. Sandeep K. Singh


Dr.Richa Dubey


Jagriti Chaturvedi


Mangi Lal Godara


Manish Kumar


Manjeet Gupta


Manveer Patel


Md Emdadul Hoque


Md Mahamudul Hassan


Navneet Dwivedi


Nikhil Gupta


Pranjali


Rajeev Kumar Verma


Renuka Ranjan


Saikat Jati


Saiket Guria


Sandip Kr. Das


Satyajit Roy


Sayan Dey


Shagufa A. Ehtesham


SK Abu Saleh


Sourabh Yadav


Sourav Pramanik


Subrata Das


Swarnima Pandey


Swarup Senapati


Tanaya Manna


Tarun Mahata


Tazeen


Tishyasaumya Bera


Vandana Jaiswal

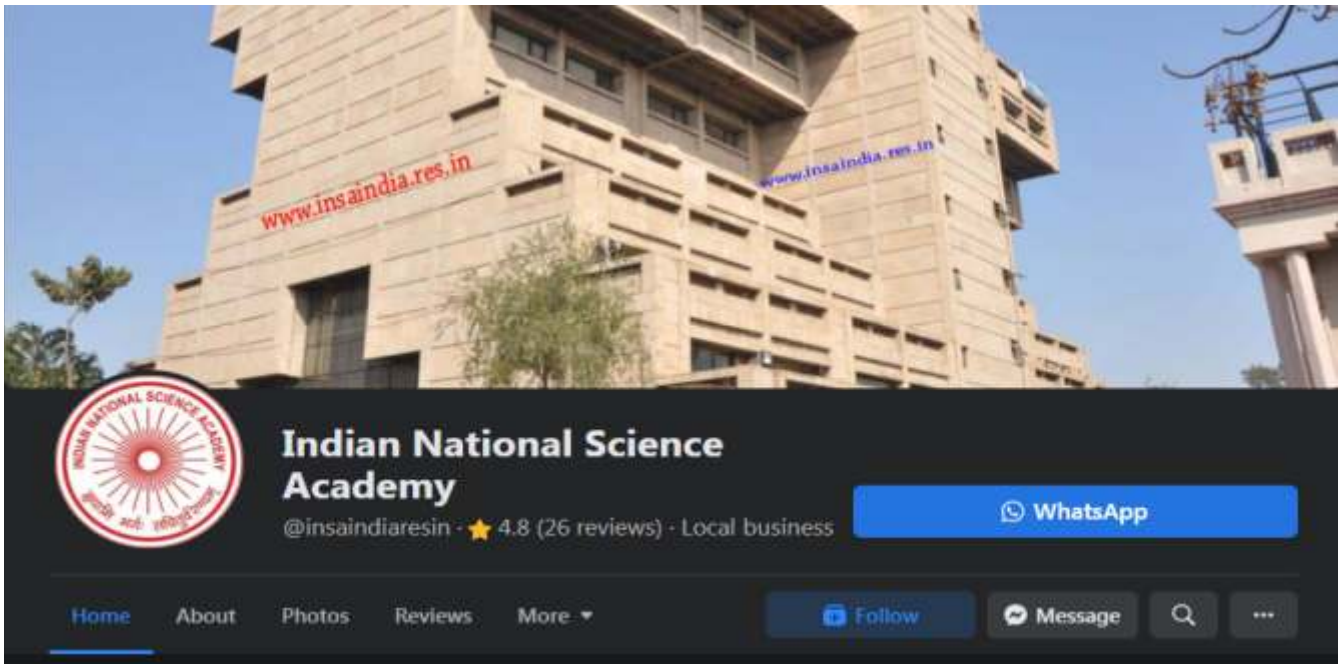

Vikram Singh

# Superannuation

**Dr. Raja Roy**
Professor
(Director, Additional Charge)
June 2020

# Obituary

Centre of BioMedical Research family deeply mourns the demise of Professor C.L. Khetrapal, Founder Director, CBMR




Prof. Chunni Lal Khetrapal

Prof. Chunni Lal Khetrapal (b.1937) breathed his last this morning, July 21, 2021 at Lucknow.

A product of Allahabad University, Dr. Khetrapal joined the prestigious Atomic Energy Establishment Training School at Mumbai (1959) and then the Tata Institute of Fundamental Research (TIFR), Mumbai. After PhD, awarded by Bombay University (1965), he researched at a number of institutions abroad such as University of Basel, Switzerland (1967-69); Liquid Crystal Institute, and Kent State University, Kent, USA (1971-72). He joined Raman Research Institute at Bengaluru (1973) as Associate Professor. In the year 1984, he moved as Professor and Head, Sophisticated Instruments Facility at Indian Institute of Science, Bangalore (1984-98). He also worked at NIH, Bethesda, Maryland, USA (1979-80 and 1984). In the year 1998, he was appointed as Vice-Chancellor of the Allahabad University (1998-2001). After that he joined Sanjay Gandhi Post-graduate Institute of Medical Sciences, Lucknow as Distinguished Professor (2001-06); and was founder-Director, Centre of Biomedical Magnetic Resonance, Lucknow.

Nuclear Magnetic Resonance (NMR) was the chosen field of research of Prof. Khetrapal. His contributions in NMR have literally opened new avenues of research. Professor Khetrapal was an institution builder and took lead in establishing the first National Centre on NMR in Bangalore and the Centre of Biomedical Magnetic Resonance in Lucknow. At the University of Allahabad, he initiated several new academic programmes and created two institutes and several Centres of Excellence. He has over two hundred and sixty publications to his credit and authored several reviews, books, chapters in books and monographs.

Among Professor Khetrapal's honours and awards are: SS Bhatnagar Prize (1982), RK Asundi Memorial Lecture Award of INSA (1990); President, Physical Sciences and of Chemistry Section of Indian Science Congress (1994); CV Raman Award of UGC (1996); Goyal Prize (1996); JC Ghosh Lecture Award of Indian Chemical Society (1998); PC Ray Memorial Medal of the Indian Science Congress Association (2002); Life time Achievement Award of the Indian Chemical Society (2005) and NR Dhar Memorial Lecture Award of National Academy of Sciences (India), Allahabad (2005).

He was a Member of International Council of Magnetic Resonance in Biological Systems (1984-94) and of Governing Council, the International Society of Magnetic Resonance (1986-95). He was the Founder-President of the National Magnetic Resonance Society. He was a member of the International Editorial Board of prestigious series of publications in NMR. In addition to INSA, he was Fellow of the National Academy of Sciences at Prayag ((also its Vice-President, 1999-2000). He was serving on the INSA Sectional Committee-III

His demise is a big loss to the scientific community. INSA family deeply mourns the loss and conveys heart-felt condolences to his family.

# CBMR research was generously supported by the U.P. Government

## Funding

Rs. in Lakhs

| | |
|---|---|
| UP Government | 1580.00 |
| Extramural Funding | 342.46 |
| Total | 1922.46 |

# Extramural Projects funding Agencies

ICMR
INDIAN COUNCIL OF MEDICAL RESEARCH

iNSERB
DIA

सत्यमेव जयते
Department of Science and Technology
Ministry of Science and Technology
Government of India

सत्यमेव जयते
Department of BioTechnology Government of India

ज्ञान-विज्ञान विमुक्तये
University Grants Commission

सत्यमेव जयते
Ministry of Earth Sciences
Government of India

CSIR INDIA

BARC

DRDO
DEFENCE R&D ORGANISATION
MINISTRY OF DEFENCE
DRDO


CENTRE OF BIOMEDICA